Original research

Access to Innovative Medicines Nusinersen, Onasemnogene Abeparvovec, and Risdiplam in Low- to Middle- Income Countries

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Abstract

The recent marketing approval of nusinersen, risdiplam, and onasemnogene abeparvovec by the Food and Drug Administration and the European Medicines Agency has revolutionized access to care for spinal muscular atrophy patients. However, their high prices have raised concerns in several countries about patients and governments' ability to pay for these medicines, especially in low- and middle- income countries. Since on-time access to these medicines has a significant impact on quality of life, and psychosocial health, this study aimed to identify access to medicines, epidemiology, diagnosis, onset, and regulatory and health technology assessment frameworks for spinal muscular atrophy in low- and middle- income countries. An analysis of publicly available literature and interviews with key spinal muscular atrophy stakeholders, including patient and families' organizations and a pharmaceutical companies' consultant, was performed. Overall, there was a lack of access to spinal muscular atrophy medicines in low- and middle- income countries. Main reasons were high cost of spinal muscular atrophy medicines, lack of efforts from companies and governments, lack of reimbursement for these medicines, and lack of reach in companies' humanitarian programs. Most families and patients from Bangladesh, Bolivia, Indonesia, South Africa, Tunisia, and Ukraine reported a high economic burden, a lack of understanding among clinicians of the disease, and fluent conversations with pharmaceutical companies but not with their respective governments. In conclusion, there was an overall lack of access to spinal muscular atrophy in low- and middle- income countries, although regional differences were observed. Capacity building, cross-national training programs, and global health partnerships could help clinicians in low- and middle- income countries to identify early spinal muscular atrophy symptomatology. Moreover, the creation of an Essential Medicines List for rare diseases could allow the democratization of orphan medicines.

Layman Summary (500 words)

The recent commercialization of nusinersen, risdiplam, and onasemnogene abeparvovec by the American and European regulatory medicine agencies has revolutionized access to treatment for spinal muscular atrophy patients. However, their high prices have raised concerns in several countries about patients and governments' ability to pay, especially in low- and middle- income countries. Since access to spinal muscular atrophy medicines contributes heavily to the physical and mental well-being of patients, this research tried to study how patients in low- and middle-income countries had access to spinal muscular atrophy medicines, and how the diagnosis and the identification of the symptoms associated with the disease influenced the identification of spinal muscular atrophy patients. In order to conduct the research, publicly available data and interviews with patient and families' organizations and a pharmaceutical companies' consultant were held. In general, it was observed a lack of access to spinal muscular atrophy medicines due to their high cost, lack of efforts from companies and governments, and lack of impactful humanitarian programs. Families and patients expressed concerns on the high economic cost of these medicines, lack of training among clinicians on spinal muscular atrophy, and lack of fluent conversations with their respective governments. In conclusion, there was an overall lack of access to spinal muscular atrophy in low- and middle- income countries, although regional differences were observed. The creation of infrastructure in low- and middle- income countries, training programs for clinicians working in low- and middle- income countries, and global health collaborations between international stakeholders could help clinicians in low- and middle- income countries to identify earlier the spinal muscular atrophy symptomatology. Moreover, the creation of an Essential Medicines List for rare diseases could allow the democratization of orphan medicines.

Introduction

Spinal Muscular Atrophy (SMA) is an autosomal recessive progressive motor neuron disorder caused by loss-of-function mutations on chromosome 5 (5q).[1,2] In 95% of SMA cases, SMA is caused by deletions in exon 7 in survival motor neuron 1 (*SMN1*) gene.[1,3] This deletion avoids the formation of the functional full-length form of the SMN protein.[1] Survival motor neuron 2 (*SMN2*) shares a high degree of similarity with *SMN1*, but produces a truncated SMN protein without exon 7.[1,3] However, around 10-15% of *SMN2* transcripts produce a SMN protein functional.[1,2] Thereby, the copy number of *SMN2* gene is correlated with the severity of the disease.[1]

The prevalence of people living with SMA is about 1-2 cases per 100,000, and the incidence is around 1 in 10.000 births.[2] However, there are differences across countries and populations. In a systematic review, the groups with higher carrier frequency were Asians, Indians, Caucasians, and Arabs.[4] In contrast, Hispanic, and Sub-Saharan population had the lower carrier frequencies.[2,4] However, Hispanic societies are genetically very diverse.[4] In a study performed in Cuba it was found that Caucasian population was largely more affected than Sub-Saharan descendent population in the country.[5] However, it has been suggested that SMA prevalence and incidence in the Sub-Saharan descendant population can be under-estimated.[2,6] Several studies have shown some subjects have two copies of *SMN1* gene in only one of the alleles.[7,8] This feature is common in sub Saharan descendant population.[6] As current carrier identification techniques rely on the number of copies of the gene, these subjects are not identified as carriers of the disease, leading to an overall underestimated incidence and prevalence on these populations.[6]

Classic treatment for SMA has widely consisted of best supportive care until the development of innovative medicines.[1] Nusinersen, commercialized as Spinraza by Biogen, was the first SMA treatment to receive marketing authorization in the United States (US) and Europe.[9,10] Nusinersen

is an antisense oligonucleotide that attaches to a target in intron 7 in *SMN2* gene.[1] This attachment inhibits splicing factors, allowing the integration of exon 7 in the mRNA, enhancing the production of full-length SMN protein.[9] Onasemnogene abeparvovec, commercialized as Zolgensma by Novartis, was the second SMA treatment authorized by the US' Food and Drug Administration (FDA).[11] Onasemnogene abeparvovec is a gene therapy treatment using adeno-associated virus (AAV) 9 vector-based technology.[1,11] AAV9 has tropism for the central nervous system and muscle and it is used to deliver the full-length functional SMN protein into target motor neuron cells.[11] Risdiplam, commercialized as Evrysdi by Roche, was the third SMA treatment approved in the US and Europe.[1,12] Similarly to nusinersen, risdiplam modulates *SMN2* splicing, producing full-length SMN protein.[10]

Concerns about the price of these technologies, especially onasemnogene abeparvovec, have risen in several countries, including the US and the Netherlands.[13,14] Although access in high income countries appears to be challenging, it is expected that insurance systems can afford it.[11] However, several actors as the Bill & Melinda Gates Foundation are worried access to innovative gene therapies is not equalitarian and low- and middle- income countries (LMICs) are left behind.[13]

The primary objective of the study was to collect publicly available data on SMA in LMICs, including access to medicines, epidemiology, diagnosis, onset, and regulatory and health technology assessment (HTA) frameworks. The secondary objective was to delve into the aforementioned topics by interviewing key SMA stakeholders, including patient and families' organizations and pharmaceutical companies' consultants.

Methods

Scoping review

Academic and grey literature were identified following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 checklist and flow diagram, as well as the PRISMA extension for scoping reviews.

Eligibility criteria

Literature discussing SMA, as well as the use of risdiplam, nusinersen and onasemnogene abeparvovec in LMICs, including low-income countries (LIC), lower-middle-income countries (LMICs), and upper-middle-income countries (UMIC), was considered. An overview of the countries and their classification included is found in table S1. In addition, only documents written in a language understood by researcher Madrid Paredes, J. (English, French, Portuguese, and Spanish) and that were available through the Utrecht University Library were included. Documents that did not discuss SMA or were focused on high-income countries (HIC) were excluded. In addition, the records needed to provide a relevant overview on the state of the topic for SMA in these countries.

Information sources

Embase was selected as the search engine for obtaining academic literature, while Overton was selected for obtaining both academic and grey literature. Both search engines were searched until 23 June 2023.

Search strategy

The search terms included LMICs, “Spinal Muscular Atrophy”, “Nusinersen”, “Onasemnogene Abeparvovec” and “Risdiplam”. Variations were included with the Boolean operators “AND” and “OR”. In an additional search strategy, Overton’s source filters were used to only obtain records with LMIC as source countries. An overview of the search strategy is found in annex 1.

Selection process

Records from Embase and Overton were imported to Endnote to eliminate duplicates from the selection. Consequently, records were imported to ASReview, which machine learning algorithms were used to facilitate the screening of records based on title and abstract. The records were reviewed exclusively by Madrid Paredes, J. Records not written in English, French, Portuguese, and Spanish were excluded, as well as those that were not accessible through Utrecht University Library. Only records that were providing a relevant overview of SMA in LMIC were included.

Data collection and outcome definition

Data about SMA and use of nusinersen, onasemnogene abeparvovec, and risdiplam was collected by Madrid Paredes, J. by reading the full text of the records. No automatic tools were used to collect data. As a scoping review, outcomes and classifications were defined through the process.

Data synthesis

A flowchart was included to summarize the decision-making process during the selection process. The records included were overviewed in tabular format.

Interviews

Setting and participants

Between September and November of 2023, emails were sent to key SMA stakeholders (n=36), including patient and families' organizations operating in LMICs, experts in SMA, and pharmaceutical company's consultants to invite them to participate in the study. For those that replied, an informed consent form, and the interview protocol were sent. Only organizations that signed the information consent form were eligible to participate in the study. A copy of the interview protocol and the informed consent form can be found in annex 2 and 3. Interviews with key stakeholders were held until 1 December 2023.

Data collection

An interview protocol was created to address the gaps identified in the scoping review. Participants were asked to provide information on 4 blocks consisting of treatment and access, epidemiology and genetics, stakeholders' interactions, and onset and diagnosis.

The first block consisted of 2 questions, and 7 subquestions. It covered existing SMA guidelines, access to SMA treatments, reimbursement of SMA drugs, best supportive care, humanitarian programs, registration/marketing authorization prospect of SMA drugs, and the reimbursement system in the country of interest. The second block consisted of 1 question, and it covered the epidemiology and genetics of SMA. The third block consisted of 2 questions, and 2 subquestions. It covered the communications and the nature of these communications between the key stakeholders for access to SMA medicines: patient and families' organizations, governments, and companies. The fourth block consisted of 2 questions. It covered access to diagnostics, and diagnosis type in the country. Given the nature of the project being a study of stakeholder's perceptions, participants were encouraged to answer freely.

Data synthesis

Interviews responses were analyzed qualitatively using Microsoft Word. The responses were organized into four categories: treatment & access, best supportive care, epidemiology, onset, and diagnosis, and organization, government, and company interface. The interview responses were overviewed in tabular format.

Results

Scoping review

Data selection

Embase and Overton searches yielded 183 and 815 records, respectively, accounting for a total of 1,008 records. Of the 1,008 identified records, 69 duplicates were removed. Of the 939 remaining records, 177 were marked as relevant and assessed for eligibility. Of them, 90 records met the eligibility criteria. From the 87 records excluded: 22 were based on HIC, 17 were mainly focused on pathological aspects of SMA, 13 were marked as irrelevant, 12 were mainly focused on genetics, 7 were in languages not understood by the researcher, 4 were neither focused on LMICs nor SMA, 3 were mainly focused on the clinical aspects of the disease, 3 were focused on diseases other than SMA, 3 were only mentioning the SMA disease classification, and 2 were mainly focused on sociology aspects. The study selection process is summarized in figure 1.

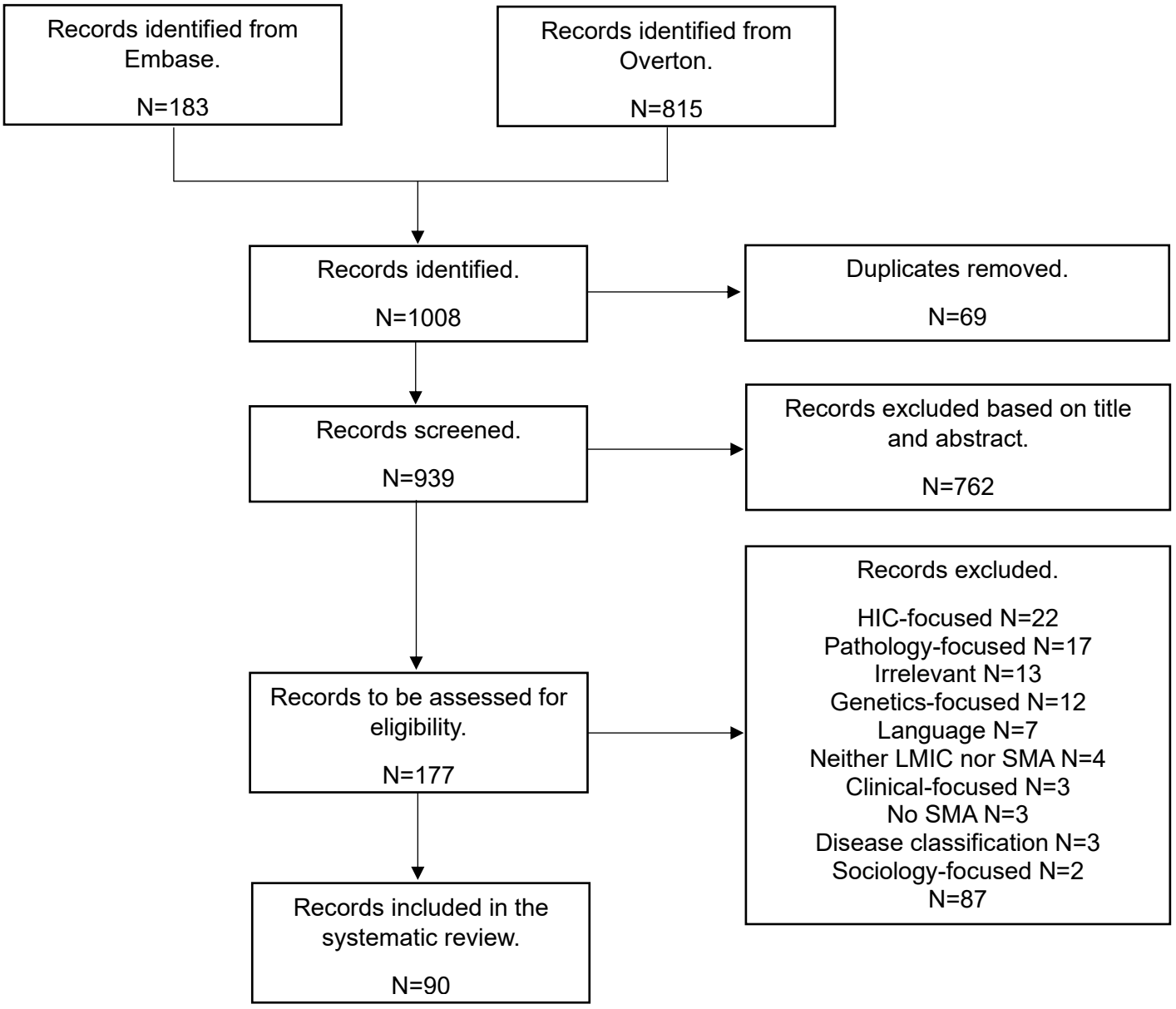

Figure 1. Study selection flow chart.

Epidemiology and genetics

The cause of SMA was related to deletions in *SMN1* gene, although there were discrepancies across studies (table S2). Studies suggested homozygous deletion of exon 7 in *SMN1* gene were the most common in Chinese SMA patients, ranging in these studies from 96.4% to 99.2%.[15,16] Studies conducted in India suggested that deletion of both exons 7 and 8 were the most common deletion in SMA patients. However, there were discrepancies across studies, ranging from 83.1% to 100%.[17–19] In addition, frequency of exons 7 and/or 8 deletions in the Iranian population was always above 90% in the studies consulted, ranging from 90% to 97%.[20–22] Deletion of exon 7 was less common in Tunisia, Venezuela, and Vietnam, with a frequency of this deletion being 45.4%,[23] 51.7%,[24] and 41.2%,[25] respectively. Interestingly, in a study conducted in South Africa, there were differences in the frequency of exon 7 deletion between black and white SMA patients, with 38% and 79%, respectively.[26]

There was a high diversity in carrier frequency and SMA prevalence and incidence across countries in the literature consulted (table S2). Carrier frequency in China ranged from 1.77% to 2.39% depending on the study.[7,27–29] Differences across populations were found, with Dai populations showing the lowest carrier frequency (0%) and Tujia the highest (4.3%).[28] A systematic review consisting of 10 studies considered an overall carrier frequency of 2% (95% CI 1.7-2.3%).[30] In a study conducted in Thailand, a similar carrier frequency was observed, with 1 in 56.1 (1.78%).[31] In Mexico and Venezuela, the carrier frequency was estimated to be 2.62% and 2%, respectively.[24,32] The study conducted in Mexico did not observe any differences between regions, and justified the differences with other studies conducted in the country with the diverse genetic background of the Hispanic population.[32] In Ukraine, the carrier frequency was estimated to be 1 in 31 (3.24%), higher than in other European countries.[33]

Other studies pointed out the relation between consanguinity and increased incidence and prevalence. Morocco (4%), and Iran (5%) presented the highest carrier frequencies due to the

high rate of consanguinity in the countries.[34,35] Similarly, it has been reported in literature the importance of carrier screening programs in Egypt due to the high rate of consanguinity in the country.[36] A study conducted in India also showed that of 96 patients included in the study, 29 were born of consanguineous relationships.[37] Another study conducted in Ghana demonstrated the relation between consanguinity and neurological disorders, including SMA.[38] Similarly, a study in Tunisia showed that consanguinity was present in 55.71% of the SMA families studied.[23]

Quality of life and comorbidities

SMA patients in LMIC suffer a high burden of disease (table S2). A study conducted in China showed that anxiety and depression were correlated with respiratory, digestive, and skeletal symptoms.[39] Another study conducted in China showed that most SMA patients included in the study had a low bone muscular density, although health bone was poorer in SMA type II than in SMA type III.[40] Most common comorbidities in Colombian SMA patients were scoliosis, hip dysplasia, and impaired motor development.[41] However, in Egypt the most common comorbidities were hypotonia, weakness and inability to walk.[42] Hypotonia was also found to be the most common comorbidity in an study performed in Indian population.[18]

Several parameters determine the quality of life of SMA patients. SMA patients with better motor function and less severe SMA showed better scores in quality of life (QoL) questionnaires,[43] while patients with limited mobility, skeleton deformity, stable course of disease, respiratory support, inability to attend school and digestive system dysfunction were associated with lower scores.[44,45] In addition, SMA type III patients scored better in physical, emotional, social, and cognitive domains than type I and II patients in China and in Thailand,[44,45] although other study did not detect any differences between SMA type II and III in Iran.[46]

Treatment and access to care

Access to nusinersen, onasemnogene abeparvovec and risdiplam varied across LMICs (table S2). Nusinersen was available in China, Colombia, Mexico, or Brazil.[43,47–49] However, most Chinese patients did not have access to nusinersen due to the lack of reimbursement.[39] As of 2023, nusinersen was the only marketed treatment in Colombia.[47] In addition, best supportive care was the only available strategy for managing SMA in Mexico before the introduction of nusinersen in 2019.[48] Although treatments were available in some countries, most countries in Latin America did not have access to SMA medicines and care.[50] Indian patients had received nusinersen, onasemnogene abeparvovec and risdiplam through humanitarian access programs, but they were not reimbursed.[51–53] However, risdiplam received recently marketing approval by the Drug Controller General of India.[53] In addition, as of 2020, risdiplam was in pre-registration phase in several countries, such as Brazil, China, or Indonesia.[54] Egypt's National Drug Authority approved the use of risdiplam in June 2021. On other hand, Brazil's drug pricing authority stablished a maximum price for onasemnogene abeparvovec that was 77% lower than the price set by Novartis, what led to Novartis deciding not to commercialize the medicine in the country.[55]

Several studies conducted in China reported that treatment with nusinersen was associated with higher quality of life scores.[43,44] Another study conducted in Colombia showed psychosocial health score improved in patients treated with nusinersen, but no differences in the physical health score was observed.[56] However, both patient responsibility and financial burden increased.[56] Moreover, treatment with the non-disease modifying drug pyridostigmine improved distal tremor and lingual fasciculations, improving quality of life of patients.

Regulatory and health technology assessment context

The regulatory and health technology assessment (HTA) context was different across the countries (table S2). A budget impact analysis showed the potential inclusion of nusinersen on the Chinese basic medical insurance would have limited impact but improve access.[57] However, comparisons between SMA treatments positioned risdiplam before nusinersen. A cost-effectiveness assessment showed patients treated with risdiplam in China had 1.42 more life-years and 1.41 more Quality-adjusted life years (QALYs).[58] Similarly, a budget impact analysis performed in Colombia showed nusinersen was associated with higher costs in comparison with risdiplam due to the cost of treatment, concomitant medicines, and management strategies.[59] Economic burden was studied in Mexico. Although yearly cost of managing SMA patients type I were higher, the longer life expectancy of SMA type II and III made the financial impact broader.[60]

Nusinersen was incorporated in Brazil through a risk-sharing purchasing modality.[61] Other treatments targeting SMA have used the special procedure for rare diseases RDC 205/2017 in Brazil, which guarantees flexibility in technical requests and encourages submission in different regions.[62] In addition, both nusinersen and onasemnogene abeparvovec are exempt in the country from taxes on transactions.[63] The Ukrainian Minister of Health addressed risdiplam's applicant to negotiate a managed entry agreement,[64] what led to risdiplam to be procured centrally for the treatment of children with SMA.[65] In addition, nusinersen was not included in the health services and technologies financed from the maximum budget in Colombia.[66]

Records characteristics

Of the 90 records included, 76 were academic and 14 were grey literature (table 1). The most common topic found was epidemiology, with 38 records, genetics, with 28, treatment access to care, with 27, quality of life and comorbidities, with 18, diagnosis, with 7, (patient, family and public) perspectives, with 6, regulation, with 3, and policy, with 1. In total, records focused on 31

different countries. Of the 90 records, 21 were focused on China, 14 on Brazil, 11 on India, 8 on Iran, 7 on Colombia, 4 globally and in Mexico, 3 on Indonesia, South Africa, and Ukraine, 2 on Egypt, Pakistan, Thailand, Morocco, and Venezuela, and 1 on Armenia, El Salvador, Ghana, Guatemala, Honduras, Moldova, Mongolia, Nicaragua, North Africa, Paraguay, Peru, Sri Lanka, Tunisia, Vietnam, West Africa, and Yemen. This accounted for 56 records being focused on upper-middle income countries, 39 on lower-middle income countries, 5 on supranational jurisdictions, 2 on non-classified countries, and 1 on a low income country. Concerning the geographic region, 27 were focused on East Asia and Pacific, 24 on Latin America and Caribbean, 15 on Middle East and North Africa, 14 on South Asia, 5 on Europe and Central Asia and Sub Saharan Africa, 4 globally, and 4 globally.

Table 1. Records description

Characteristics	N
Type of literature	
Academic	76
Grey	14
Topic*	
Epidemiology	38
Genetics	28
Treatment and access to care	27
Quality of life and comorbidities	18
Health technology assessment	9
Diagnosis	7
Perspectives	6
Regulation	3
Policy	1
Country*	
China	21
Brazil	14
India	11
Iran	8
Colombia	7
Global	4
Mexico	4
Indonesia	3
South Africa	3
Ukraine	3
Egypt	2
Pakistan	2
Thailand	2
Morocco	2
Venezuela	2
Armenia	1
El Salvador	1
Ghana	1
Guatemala	1
Honduras	1
Moldova	1
Mongolia	1
Nicaragua	1
North Africa	1
Paraguay	1
Peru	1
Sri Lanka	1
Tunisia	1
Vietnam	1
West Africa	1
Yemen	1
Classification	
Upper-middle income country	56

Lower-middle income country	39
None/not classified	7
Low income country	1
Geographic region	
East Asia and Pacific	27
Latin America and Caribbean	24
Middle East and North Africa	15
South Asia	14
Europe and Central Asia	5
Sub Saharan Africa	5
Global	4

* More than one category can apply

Interviews

Stakeholder selection

Of the 36 stakeholders consulted, 14 replied (39%) and 7 (19%) of them sent the signed informed consent back. Of this, 6 (86%) were representatives from patient and families' organizations, and 1 (14%) was a pharmaceutical companies' consultant. Informal talks were held with experts on SMA. The patient and families' organizations operated in Bangladesh (LMIC, South Asia), Bolivia (LMIC, Latin American & Caribbean), Indonesia (UMIC, East Asia & Pacific), South Africa (UMIC, Sub-Saharan Africa), Tunisia (LMIC, Middle East & North Africa), and Ukraine (LMIC, Europe & Central Asia).

Treatment & Access

Availability of SMA medicines and the different access strategies employed in the countries where the patient and families' organizations operated is summarized in tables 2, S3, and S4.

Access to SMA medicines was scarce in all LMICs (table 2). However, some differences were observed. Risdiplam was the only marketed medicine in Bangladesh, Indonesia, and South Africa. However, the medicine was not reimbursed by either public or private insurances. Patients had only had access to risdiplam in these countries through compassionate use programs in

Bangladesh, and South Africa, and through post-trial access strategies in Indonesia. In Ukraine, risdiplam was both marketed and reimbursed for the treatment of SMA type I patients. Moreover, there was an ongoing assessment by the Ukrainian Agency for Health Technology Assessment to recommend nusinersen for reimbursement for the treatment of SMA type II patients. In Tunisia, there was an ongoing assessment by the Tunisian National Health Insurance Fund in collaboration with different Ministries (Finance, Social Affairs, and Health) to market risdiplam. Nusinersen was only marketed in Ukraine, where there was an ongoing assessment by the Ukrainian Agency for Health Technology Assessment to recommend it for reimbursement for SMA type II patients. However, Ukrainian patients had only had access to nusinersen through the limited donation programs during 2022-2024. Biogen expressed in the past their interest in registering its medicine in Bangladesh, however there was no evidence it was doing so in the other countries. Moreover, Biogen expressed the main obstacle to registering nusinersen in South Africa was the non-inclusion of SMA in the prescribed minimum list. Onasemnogene abeparvovec was not marketed in any of the countries included. However, there was an ongoing assessment in Ukraine to authorize onasemnogene abeparvovec in the country. Onasemnogene abeparvovec has only been accessible to patients in Bangladesh and Tunisia through the global managed access program organized by Novartis, and in South Africa through the clinical trial that is currently being held at the Red Cross War Memorial Children's Hospital in Cape Town.

Humanitarian programs were a common practice in most countries included (table 2). Companies tended to prioritize countries with a low gross domestic product per capita and a high prevalence of disease to implement their humanitarian programs (table S4). In contrast, companies considered different criteria to market their products, i.e., governments' abilities to pay, presence of specialized clinical facilities, and trained clinicians to administer their medicines. Moreover, in South Africa, patients could access non-marketed medicines through section 21A (table S3). However, no SMA patient had benefited from this pathway due to complications of the

bureaucratic process and the high cost of SMA medicines. This was consistent with patients paying out-of-pocket for imported drugs at U.S. prices (table S4). In addition, clinical trials had been performed only in South Africa (table 2). For rare diseases, companies usually run global clinical trials across countries to ensure enrolling a significant number of patients (table S4). However, other factors also played a role in their rationale for selecting the location for their clinical trials, i.e., presence of clinical experts, commercial interests, high-quality medical facilities, or key opinion leaders.

Best supportive care

Best supportive care was the standard of care in all countries where the patient and families' organizations operated but in Ukraine (Table 2).

Reimbursement of best supportive care ranged from no reimbursement (Bangladesh) to partial reimbursement (Bolivia, Indonesia, and South Africa), and full reimbursement (Tunisia). In Bolivia and South Africa, private insurance companies reimbursed partially certain BSC therapies. However, in South Africa, there were disparities in healthcare infrastructure across the country, resulting in significant differences in patient access to BSC depending on the region. In contrast, Indonesian and Tunisian SMA patients had access to BSC through their respective public health insurances. In all countries but in Tunisia and Ukraine (no data), parents and families needed to pay for the equipment out-of-pocket.

Epidemiology, Genetics, Onset & Diagnosis

Overall, the epidemiology of SMA in the countries included was difficult to determine due to delays in diagnosis, and lack of newborn screening (NBS) programs, and reimbursement for genetic tests (table 2).

In all countries but in Tunisia there were established patient registries. Diagnosed SMA patients ranged from 15 (Bolivia), South Africa (30), 162 (Bangladesh), 256 (Indonesia), to 350-450 (Ukraine). From 2022, Ukraine was the only country with an active NBS program. However, there were ongoing conversations in Tunisia to launch an NBS study pilot. Moreover, reimbursement of genetic tests ranged from no reimbursement (Bangladesh, Bolivia, Indonesia), partial reimbursement (Tunisia), and full reimbursement (South Africa, Ukraine). In Bolivia, Indonesia, South Africa, Tunisia, and Ukraine, national genetic centers for SMA diagnosis were available. In contrast, Bangladeshi patients and parents needed to send their blood samples to India. Although genetic centers were available in Bolivia and South Africa, it was a common practice for patients and families to get their diagnosis abroad.

Organization, Government & Company Interface

Overall, patients' organizations had more fluent conversations with companies than with their respective governments, where tensions were common (table 2).

Communication between SMA patient and families' organizations and governments ranged from none (Bangladesh, Bolivia, South Africa, Tunisia, and Ukraine) to fluent communications (Indonesia) (table 2). In Indonesia, patient and families' organizations were lobbying to include risdiplam in the national drug formularies list and to reimburse genetic tests, but the response of the government had been negative. Moreover, Bangladeshi, Tunisian, and Ukrainian organizations had tried to engage in conversations with their respective governments. In contrast, communications with companies had been more fluent (table 2). Biogen had meetings with the Bangladeshi, South African, and Ukrainian patient, and families' organizations. Novartis with all organizations but the Bolivian, and Roche with all but the South African. Collaboration and communication between patient and families' organizations and companies consisted on access to SMA medicines (Indonesia, South Africa), advice to generate funds (Bangladesh), information

on humanitarian programs (Indonesia), launch of new programs (Tunisia), participation in clinical trials (South Africa), registration of SMA medicines (Tunisia), and sponsorship (Tunisia).

Table 2. Summary of interviews with patient and families' organizations

		Bangladesh	Bolivia	Indonesia	South Africa	Tunisia	Ukraine
	Geographic region	South Asia	Latin American & Caribbean	East Asia & Pacific	Sub-Saharan Africa	Middle East & North Africa	Europe & Central Asia
Treatment & Access	**Guideline**	No	No	No	No	No	No
	Treatment						
	Risdiplam						
	Marketing authorization	Yes	No	Yes	Yes	No	Yes
	Reimbursement	No	No	No	No	No	Yes
	Humanitarian programs	Yes	No	No	Yes	Yes	No
	Other form of access	No	No	Yes	No	No	No
	Nusinersen						
	Marketing authorization	No	No	No	No	No	Yes
	Reimbursement	No	No	No	No	No	No
	Humanitarian programs	No	No	No	No	No	Yes
	Other form of access	No	No	No	No	No	No
	Onasemnogene ab.						
	Marketing authorization	No	No	No	No	No	No
	Reimbursement	No	No	No	No	No	No
	Humanitarian programs	Yes	No	No	No	Yes	No
	Other form of access	No	No	No	Yes	No	No
BSC	**Best supportive care**						
	Standard of care	Yes	Yes	Yes	Yes	Yes	No
	Reimbursement	No	No/Partially	Yes/Partially	No/Partially	Yes	NA
Epidemiology, Onset & Diagnosis	**Epidemiology**						
	Number	162	15	256	30	NA	350-450
	Diagnostic						
	Newborn screening	No	No	No	No	No	Yes
	Diagnostic test						
	Reimbursement	No	No	No	Yes	No	Yes
	Location	Abroad (India)	Nationally or abroad	Nationally	Nationally or abroad	Nationally	Nationally
Organization, Government & Company Interface	**Government**						
	Meeting	No	No	Yes	No	No	No
	Company						
	Biogen						
	Meeting	Yes	No	No	Yes	No	Yes
	Financial relationship	No	NA	NA	No	NA	No
	Novartis						
	Meeting	Yes	No	Yes	Yes	Yes	Yes
	Financial relationship	No	NA	No	No	Yes	No
	Roche						
	Meeting	Yes	Yes	Yes	No	Yes	Yes
	Financial relationship	No	No	No	NA	No	No

Discussion

The aim of this study was to i) collect publicly available data on SMA in LMICs, including access to SMA medicines, epidemiology, diagnosis, onset, and regulatory and HTA frameworks, and ii) fill the gap in literature by delving into the aforementioned topics by interviewing patient and families' organizations and a pharmaceutical companies' consultant. This study adds to the body of literature that describes SMA across LMICs, but delving into patient and families' perspectives on access, epidemiology, diagnosis, and relation with stakeholders.

Main findings

Overall, there was a lack of access to SMA medicines in LMICs. Main reasons for lack of access were high cost and subsequent unaffordability of SMA medicines, lack of efforts from companies and governments, lack of reimbursement for SMA medicines, and lack of reach in companies' humanitarian programs. Previous literature showed SMA medicines were authorized in China, Colombia, Mexico, or Brazil with different levels of reimbursement.[43,47–49] However, in all countries where the interviewed patient and families' organizations operated but in Ukraine, there was a lack of reimbursement for SMA medicines (Table 2 and S3), showing a high-level of variability across LMICs. Having appropriate treatment a significant impact on patients' quality of life and psychosocial health,[56] equal on-time access to SMA medicines is of high importance. Consequently, BSC was the standard for care in most LMICs, with patients and families generally needing to pay for the equipment and the BSC out-of-pocket (Table 2 and S3). Although all companies had humanitarian programs in place, patient and families' organizations reported more efforts were needed to ensure access to SMA medicines.

In the literature differences in disease genetics across ethnic groups were identified. A study performed in South Africa showed homozygous deletions in *SMN1* gene were more common in Caucasian SMA patients than in Sub-Saharan SMA patients, suggesting the role of neighboring

genes as *NAIP*.[26] Similarly, several studies conducted in East Asia and South Asia showed *SMN1* deletions were not as common as in Caucasian populations,[25,67] and less than one third of the patient population in India, Pakistan, and Sri Lanka were eligible for onasemnogene abeparvovec.[67–69] Considering current medicines are focused on the insertion (onasemnogene abeparvovec),[11] or the modulation of *SMN2*-splicing (nusinersen, risdiplam)[1,10] to obtain the full-length functional copy of the SMN protein, further research is needed to elucidate how genetic differences across ethnic groups influences SMA medicines efficacy. Moreover, carrier frequency was higher in Caucasian, and east Asian populations,[7,27–29,33] although evidence showed high rate of consanguinity increased the prevalence and incidence of rare diseases, including SMA.[23,34–38] However, exact statistics in the countries where interviewed organizations operated were difficult to determine due to the lack of NBS programs, reimbursement for genetic tests, specialized healthcare infrastructure, and understanding of the disease within clinicians.

Fluent conversations between patients and families' organizations and companies were observed, however they did not always translate into access (Table 2 and S3). It was a common practice for companies to engage in conversations with these organizations to foster the marketing of their medicines (Table S4). Related to this, it was well-documented in literature how Brazilian SMA patient organizations sued the Government to have access to onasemnogene abeparvovec,[55] showing the important role these organizations play in access to medicines. However, from all countries where the interviewed organizations operated, only in Indonesia conversations between patient and families' organizations and Government were fluent (table 2 and S3). However, these conversations did not translate into reimbursement for SMA medicines and genetic tests.

Recommendations

Lack of understanding of SMA and its symptomatology within clinicians was reported as one of the reasons for misdiagnosis and undiagnosis (table 2 and S3). Initiatives as capacity building, community engagement, cross-national training programs, and global health partnerships on SMA could help clinicians in LMICs to precisely identify early SMA symptomatology and allow an on-time diagnosis. In addition, the WHO Model List of Essential Medicines or Essential Medicines List (EML) provides a list of the minimum medicines required in healthcare systems based on their efficacy, safety, and cost-effectiveness.[70] Risdiplam was proposed and contemplated for inclusion as a low production cost yet high price medicine[71,72] but it was ultimately not included in the last iteration of the Essential Medicines List (EML).[70] As the inclusion of risdiplam would result in commercial prices being closer to the manufacturing costs, further pressure is needed to ensure affordability.[71,72] Parallelly, it has been suggested the creation of an Essential Medicines List for rare diseases,[73] which could allow the democratization of orphan medicines in a context where pharmaceutical companies are increasingly investing in these medicines.

Strengths & Limitations

The analysis of the literature available was strengthened with interviews with key SMA stakeholders, including patient and families' organizations and a pharmaceutical companies' consultant. The interviews provided an in-deep insight into different facets of SMA in LMICs, including access to BSC, diagnosis, and SMA medicines, as well as the role of patient and families' organizations in influencing access. In addition, the interviewed organizations operated in countries from all geographic areas, allowing the identification of geographical differences. Furthermore, interviewees were encouraged to provide their opinions and perspectives freely, fostering communication between interviewer and interviewee.

However, the study would have been strengthened with interviews with other key stakeholders, including representatives from pharmaceutical companies and governments. This inclusion would have facilitated the identification of challenges and facilitators for access to SMA medicines in LMICs. In addition, because the interviewees came from a variety of backgrounds, there were inherent differences in the interviews.

Conclusion

There was a high variability in access and reimbursement in the LMIC, but there was an overall lack of access to SMA medicines. Main barriers to access were high cost of spinal muscular atrophy medicines, lack of efforts from companies and governments, lack of reimbursement for these medicines, and lack of reach in companies' humanitarian programs. Capacity building, cross-national training programs, and global health partnerships could help clinicians in low- and middle- income countries to identify early spinal muscular atrophy symptomatology. Moreover, the creation of an Essential Medicines List for rare diseases could allow the democratization of orphan medicines.

Supplementary figures

Table S1. Countries in scope and their classification

Country	Classification
Afghanistan	LIC
Algeria	LMIC
Angola	LMIC
Armenia	LMIC
Bangladesh	LMIC
Belize	UMIC
Benin	LIC
Bhutan	LMIC
Bolivia (Plurinational State of)	LMIC
Botswana	UMIC
Brazil	UMIC
Burkina Faso	LIC
Burundi	LIC
Cabo Verde	LMIC
Cambodia	LMIC
Cameroon	LMIC
Central African Republic	LIC
Chad	LIC
China	UMIC
Colombia	UMIC
Comoros	LIC
Congo	LMIC
Congo (Democratic Republic of the)	LIC
Côte d'Ivoire	LMIC
Djibouti	LMIC
Dominican Republic	UMIC
Ecuador	UMIC
Egypt	LMIC
El Salvador	LMIC
Equatorial Guinea	UMIC
Eritrea	LIC
Eswatini	LMIC
Ethiopia	LIC
Gabon	UMIC
Gambia	LIC
Ghana	LMIC
Guatemala	LMIC
Guinea	LIC
Guinea-Bissau	LIC
Guyana	UMIC
Haiti	LMIC
Honduras	LMIC
India	LMIC
Indonesia	LMIC
Iran (Islamic Republic of)	LMIC

Iraq	UMIC
Kenya	LMIC
Kiribati	LMIC
Korea (Democratic People's Republic of)	LIC
Kosovo	UMIC
Kyrgyzstan	LMIC
Lao People's Democratic Republic	LMIC
Lesotho	LMIC
Liberia	LIC
Madagascar	LIC
Malawi	LIC
Maldives	UMIC
Mali	LIC
Mauritania	LMIC
Mexico	UMIC
Micronesia (Federated States of)	LMIC
Moldova	UMIC
Mongolia	LMIC
Morocco	LMIC
Mozambique	LIC
Myanmar	LMIC
Namibia	UMIC
Nepal	LMIC
Nicaragua	LMIC
Niger	LIC
Nigeria	LMIC
Pakistan	LMIC
Palestine (State of)	LMIC
Papua New Guinea	LMIC
Paraguay	UMIC
Peru	UMIC
Philippines	LMIC
Rwanda	LIC
Samoa	LMIC
São Tomé and Príncipe	LMIC
Senegal	LIC
Sierra Leone	LIC
Solomon Islands	LMIC
Somalia	LIC
South Africa	UMIC
South Sudan	LIC
Sri Lanka	LMIC
Sudan	LMIC
Suriname	UMIC
Syrian Arab Republic	LMIC
Tajikistan	LMIC
Tanzania	LIC
Thailand	UMIC
Timor-Leste	LMIC
Togo	LIC
Tonga	LMIC

Tunisia	LMIC
Turkmenistan	UMIC
Tuvalu	UMIC
Uganda	LIC
Ukraine	LMIC
Uzbekistan	LMIC
Vanuatu	LMIC
Venezuela	UMIC
Vietnam	LMIC
Yemen	LMIC
Zambia	LMIC
Zimbabwe	LIC

Table S2. Main characteristics and summary of records included.

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
A comprehensive overview of SMN and NAIP copy numbers in Iranian SMA patients	2023	Academic Literature	Article	Genetics Epidemiology	Iran	LMIC	Middle East and North Africa	English Portuguese	The article studies the link between the number of copies of *SMN2* and *NAIP* genes and the SMA type. More copies of *SMN2* and *NAIP* genes were associated with less severe forms of SMA in the Iranian population. In addition, the study showed consanguinity increase the frequency of type I SMA.
Air stacking: effects on pulmonary function in patients with spinal muscular atrophy and in patients with congenital muscular dystrophy	2014	Academic Literature	Original Article	Quality of Life and Comorbidities	Brazil	UMIC	Latin America and Caribbean	English	The article studies the impact on the use of air-stacking maneuvers in the pulmonary capacity in patients with SMA type I and II. Patients showed an improvement in assisted and unassisted peak cough flow (APCF and UPFC) after using the maneuvers in a daily basis.
An Assessment of the Knowledge, Attitudes, and Practices of Patients and Families with Diagnoses of Hereditary Neuromuscular Disorders	2020	Academic Literature	Original Paper	Patient, Family and Public Perspectives	Pakistan	LMIC	South Asia	English	The paper studies the attitudes between hereditary neuromuscular disorders (NMDs) patients, including SMA patients, towards their diseases. Most patients believed NMDs were live-limiting, NMDs and SMA were curable and physical activity

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									should be avoided Unemployed and housewives' patients tend to have more knowledge of the disease than employed patients.
Anxiety and depression in school-age patients with spinal muscular atrophy: a cross-sectional study	2021	Academic Literature	Research Article	Quality of Life and Comorbidities Treatment and Access to Care	China	UMIC	East Asia and Pacific	English	The article studies the prevalence of anxiety and depression in young SMA patients. Anxiety and depression were not correlated with age, gender or SMA type, but with respiratory, digestive, and skeletal symptoms. Academic delay and low household income level were also associated with mental anxiety and depression. Of 178 patients, only 8 patients received treatment with Nusinersen. Nusinersen is the only SMA treatment available in China, but it is not accessible to most patients because it is not included insurance package.
Assessment of health-related quality of life in patients with spinal muscular atrophy in China	2022	Academic Literature	Original Article	Quality of Life and Comorbidities Treatment and Access to Care	China	UMIC	East Asia and Pacific	English	The article studies how quality of life is impacted by SMA subtype, motor function, and treatment choice in Chinese patients. Patients with less severe SMA, with better motor function, and treated by nusinersen (vs best supportive care) showed better scores in quality of life. In addition, nusinersen slowed disease

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									progression and improved quality of life after six months of treatment.
Assessment of motor function and nutritional status in children with spinal muscular atrophy treated with Nusinersen after loading period in Western China: a retrospective study	2023	Academic Literature	Research Article	Treatment and Access to Care	China	UMIC	East Asia and Pacific	English	The article studies motor function in pediatric SMA patients treated with nusinersen in Western China. The article compared motor function and nutritional status before and two months after treatment. Motor function improved for all patients, but nutritional status did not.
Birth defects in South-East Asia: a public health challenge: situation analysis	2016	Grey Literature	WHO Report	Epidemiology Diagnosis	India	LMIC	South Asia	English	The report describes the state of the topic of birth defects in South Asian countries. In India, the incidence of SMA is described to be 1:10,000. India is expanding its surveillance and genetic services to detect non-communicable diseases at birth. As part of its prevention programs for SMA, some Indian hospitals offer prenatal diagnosis using chorionic villus sampling and molecular techniques. Termination of the pregnancy in India is legal in case of genetic disorders, including SMA.
Bone mineral density and its influencing factors in Chinese children with spinal muscular atrophy types 2 and 3	2021	Academic Literature	Research	Quality of Life and Comorbidities	China	UMIC	East Asia and Pacific	English	The article studies the bone health of Chinese children with SMA types II and III. Most patients in the

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									study were diagnosed with low bone muscular density (BMD). Bone health was found to be poorer in patients with SMA type II than in patients with SMA type III. Some SMA patients presented vitamin D deficiency. The serum level of parathormone seems to be associated with BMD.
Budget Impact Analysis of Nusinersen for Spinal Muscular Atrophy in China	2023	Academic Literature	Article	Health Technology Assessment Treatment and Access to Care	China	UMIC	East Asia and Pacific	English	The article presents a budget impact analysis on the potential inclusion of nusinersen on the basic medical insurance. Nusinersen is compared with symptomatic treatment, the only available strategy in China before the approval of nusinersen in 2019. Currently, patients pay ¥ 550 000 out-of-pocket. The author emphasizes the potential inclusion of nusinersen on the medical insurance will have limited impact but improve access.
Budget Impact Analysis of Risdiplam for the Treatment of Spinal Muscular Atrophy in Colombia	2022	Academic Literature	Conference Abstract	Health Technology Assessment	Colombia	UMIC	Latin America and Caribbean	English	The conference abstract presents a budget impact analysis on the potential inclusion of risdiplam on the Colombian health system. Nusinersen and best supportive care (BSC) were compared to risdiplam. Nusinersen is associated with higher costs in

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									comparison with risdiplam due to the cost of treatment, concomitant medicines, and management strategies. The author concludes risdiplam provides an alternative treatment for SMA patients in Colombia.
Burden of disease of spinal muscular atrophy linked to chromosome 5q (5q-SMA) in Colombia	2023	Academic Literature	Original Research	Epidemiology Quality of Life and Comorbidities Treatment and Access to Care	Colombia	UMIC	Latin America and Caribbean	English	The article studies the disability-adjusted life years (DALYs) metric in Colombian SMA patients. Nusinersen is presented as the only marketed treatment for SMA. Prevalence and incidence of SMA was 0.74 and 0.1 per 100,000 habitants, respectively. Prevalence is higher for SMA type III. Total number of DALYs is 4,421 per 100,000 habitants, mostly due to premature death. Patients with SMA type I accounts for most of the DALYs.
Carrier frequency of SMA by quantitative analysis of the SMN1 deletion in the Iranian population	2010	Academic Literature	Short Communication	Epidemiology	Iran	LMIC	Middle East and North Africa	English	The article studies the carrier frequency of SMA by detecting the copy number of the deletion in *SMN1* gene in healthy Iranian individuals. Carrier frequency is estimated to be 1 in 20 (5%) in the Iranian population, being substantially higher than in the European-descendant population.

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
Carrier frequency of SMN1-related spinal muscular atrophy in north Indian population: The need for population based screening program	2020	Academic Literature	Research Letter	Epidemiology Treatment and Access to Care	India	LMIC	South Asia	English	The article calculates the carrier frequency of *SMN1* gene deletion by evaluating the data of individuals tested in the Indian state of Uttar Pradesh in the last 4 years. Carrier rate is estimated to be 1 in 38 (2.64%). Nusinersen, onasemnogene abeparvovec and risdiplam have been available for some patients in India through humanitarian access programs developed by pharmaceutical companies and SMA groups.
Carrier frequency of spinal muscular atrophy in Thailand	2019	Academic Literature	Short Communication	Epidemiology	Thailand	UMIC	East Asia and Pacific	English	The article studies the carrier frequency of *SMN1* exon 7 deletion to establish SMA prevalence in Thai population. Carrier frequency was estimated in 9/505 (1.78%), comparable to other Asian populations in previous research. The author points out the need to provide SMA testing during antenatal visits to prevent SMA. In addition, the author mentions SMA screening will allow better planning of healthcare resources, especially important in a country like Thailand, which has universal healthcare coverage.

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
Carrier Screening and Prenatal Diagnosis for Spinal Muscular Atrophy in 13,069 Chinese Pregnant Women	2020	Academic Literature	Article	Epidemiology	China	UMIC	East Asia and Pacific	English	The article tries to identify SMA carriers in 13,069 Chinese pregnant women to establish SMA prevalence in the country. Carrier frequency was estimated to be 1 in 56 (1.77%). Of women identified as SMA carriers, paternal partners were tested. For partners that both were carriers, a prenatal diagnosis was established. Only one in 13,069 fetus was diagnosed with SMA. The author mentions Nusinersen as the only therapy available in China.
Clinical and molecular characterization of patients with gross hypotonia and impaired lower motor neuron function	2012	Academic Literature	Research Brief	Epidemiology Genetics	India	LMIC	South Asia	English	The study tried to clinically and molecularly characterize patients suspected of having SMA. Prevalence was higher in males versus females in a proportion 1.5:1. SMA type I was the most prevalent form of SMA type, followed by SMA type III, II and IV. Most patients -83.1%- have a deletion of both exons 7 and 8.
Clinical characterizations of three adults with genetically confirmed spinal muscular atrophy: a case series	2022	Academic Literature	Case Report	Diagnosis Treatment and Access to Care	Indonesia	LMIC	East Asia and Pacific	English	The case report studied the cases of three different subjects with motor impairment. Two of the patients were misdiagnosed until genetic testing confirmed them to have SMA. All of them were

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									diagnosed with SMA type III. The author points out PCR technologies to test SMA are not easily accessible in Indonesia. In addition, the author mentions genetic tests are not included in the national health insurance.
Clinical Experience with Disease-Modifying Therapies in Adolescent and Adult Patients with Spinal Muscular Atrophy Type 2 and Type 3 in Mexico: Case Report	2022	Academic Literature	Case Report	Treatment and Access to Care	Mexico	UMIC	Latin America and Caribbean	English	The case report studied the intrathecal administration of nusinersen to five patients with SMA types II and III in Mexico. The case report mentions best supportive care to be the only treatment strategy before the approval of nusinersen in Mexico in 2019. Motor, ventilatory and swallowing function were studied in all patients. All patients showed an improvement in motor functions. However, advanced atrophy cannot be fully reverted.
Clinical-functional characterization of patients with spinal muscular atrophy in Central-Western Colombia	2022	Academic Literature	Original Article	Epidemiology Quality of Life and Comorbidities	Colombia	UMIC	Latin America and Caribbean	Spanish	The article tried to clinically and functionally characterize patients diagnosed with SMA in Central-Western Colombia. SMA type II was the most prevalent form of the disease (1/14), followed by SMA type III (3/14) and SMA type I (1/14). A summary of the different clinical manifestations of the disease is present. Some of the

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									most common comorbidities were scoliosis, hip dysplasia or impaired motor development.
Clinico-epidemiologic characteristics of spinal muscular atrophy among Egyptians	2010	Academic Literature	Original Article	Epidemiology Quality of Life and Comorbidities	Egypt	LMIC	Middle East and North Africa	English	The article tried to estimate SMA frequency, and clinical and molecular features of Egyptians SMA patients. Frequency was established in 17.7/100,000. SMA type I was the most frequent SMA type (60.6%) followed by type II (26.79%) and type III (8.8%). A high percentage of patients were children of consanguineous marriages (45.5%). Most common comorbidities were hypotonia, weakness, and inability to walk.
Communication of the Diagnosis of Spinal Muscular Atrophy in the Views of Patients and Family Members, a Qualitative Analysis	2022	Academic Literature	Article	Patient, Family and Public Perspectives	Brazil	UMIC	Latin America and Caribbean	English	The article analyzed SMA patients and family members perceptions towards diagnosis. Four different thematic axes were defined: clarification of the diagnosis, communication of the prognosis, affective memory, and advice to doctors. Patients and family perspectives were divided into positive and negative for each axe. Empathetic attitude, individualized communication, clarification of doubts, or providing realistic expectations are among the

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									communication needs of patients and family members with SMA.
Compassionate Treatment for Spinal Muscular Atrophy with Viral Gene Therapy: A Single Centre Experience from India	2023	Academic Literature	Conference Abstract	Treatment and Access to Care	India	LMIC	South Asia	English	The study assessed the motor improvement in children diagnosed with SMA following treatment with Onasemnogene abeparvovec. Onasemnogene abeparvovec was accessible through a global compassionate program for 11 kids, and through fundraising for 2 kids. Two weeks after treatment, all patients showed improvements in motor function, stamina, and intensity of voice. Patients diagnosed with SMA type II showed the most improvement.
Comprehensive profile and natural history of pediatric patients with spinal muscular atrophy: A large retrospective study from China	2022	Academic Literature	Original Research	Epidemiology	China	UMIC	East Asia and Pacific	English	The article presents a retrospective study of treatment naïve SMA patients in China. Motor function and clinical and genetic aspects were reviewed. SMA type II patients were the most prevalent group (175 cases), followed by type I (121), and type III (56). Most included patients (99.2%) presented a homozygous deletion in exon 7 in the *SMN1* gene. The median age of onset was influenced by the number of *SMN2* copies: 0.25 for patients

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									with 2 copies, 0.88 for patients with 3, and 1 for patients with 4 copies. A higher number of copies of *SMN2* was associated with milder forms of the disease. However, the number of copies did not always predict disease severity. SMA type IIA, IIB, and IIIA patients showed a stabilization of motor function at 5-7 years old. The same was true for SMA IIIB at 7-13 years.
Consanguinity and rare neurological disease. A five year experience from the Korle Bu Teaching Hospital, Accra, Ghana	2016	Academic Literature	Letter	Epidemiology	Ghana	LMIC	Sub-Saharan Africa	English	The letter suggests high proportion of consanguineous marriages in Northern and Ewe tribes in Ghana increase the prevalence of rare neurologic diseases, including SMA.
Constraints of carrier screening in spinal muscular atrophy: Co-existence of deletion and duplication in SMN1 gene and false negative MLPA result	2019	Academic Literature	Article	Genetics	Iran	LMIC	Middle East and North Africa	English	The article analyzed 150 families in Iran with a kid suspected of being a SMA patients. 106 families (70.66%) showed a mutation in *SMN1* gene on both alleles. Of the 106 families, 10 (9.43%) had a carrier parent with two normal copies of the *SMN1* gene (2/0 genotype). All parents inherited deletions and duplications from the grandparents. When performing a MLPA test, subjects with a 2/0 genotype will result in a false negative result. However, STR

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									markers are able to identify carriers with two copies of *SMN1* gene in one of the alleles.
Cost-Effectiveness of Risdiplam Versus Nusinersen for Treating Patients with Spinal Muscular Atrophy Type 1 in China	2022	Academic Literature	Conference Abstract	Health Technology Assessment	China	UMIC	East Asia and Pacific	English	The conference abstract evaluated the cost-effectiveness of risdiplam compared to nusinersen for patients with SMA type I. Survival and motor function were indirectly compared. Compared to nusinersen, patients treated with risdiplam had 1.42 more life-years and 1.41 more QALYs. In addition, costs of treatment with risdiplam were lower (in CNY 207,486) than treatment with nusinersen for patients with SMA type I.
Current attitudes toward carrier screening for spinal muscular atrophy among pregnant women in Eastern China	2023	Academic Literature	Original Article	Patient, Family and Public Perspectives	China	UMIC	East Asia and Pacific	English	The article studied the attitudes to SMA carrier screening among pregnant women through a 26-item survey in China. Most respondents (81.1%) would pay for undergoing an SMA carrier screening. Almost all patients (97.8%) would undergo the SMA carrier screening if it was covered by medical insurance. Of the pregnant women that said they would pay for the SMA screening, the 61.4% of them underwent it. People who had heard about SMA, with more knowledge in genetics,

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									and with higher income were more willing to have the SMA carrier screening test. Most subjects (78.4%) would prefer to obtain information about screening through physicians in hospitals. Some of the reasons to show willingness to undergo the test were to make better reproductive decisions and avoid having a child with SMA. The most recurrent reason to decline the screening was not to have a genetic disease case in the family.
Deletion analysis of spinal muscular atrophy in southern Indian population	2008	Academic Literature	Original Article	Genetics	India	LMIC	South Asia	English	The article studied the deletion of *SMN1* gene in SMA type I and II patients in Southern India. Of the SMA type I patients, 43% showed deletions in *SMN1* and/or *NAIP* genes. For SMA type II, III and IV, this percentage was 57%, 28% and 0%. In addition, the age of onset varied between subtypes. SMA type I, II and III had an age of onset of third trimester to seven months, one to two years, and three to seven years, respectively. The author concludes misdiagnoses based on clinical features can be behind the scarce correlation between *SMN1* deletion and SMA diagnosis.

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
Deletion of the SMN1 and NAIP Genes in Vietnamese Patients with Spinal Muscular Atrophy	2003	Academic Literature	Original Article	Genetics	Vietnam	LMIC	East Asia and Pacific	English	The article studies the *SMN1* and *NAIP* genes of patients clinically diagnosed with SMA. Deletion of exon 7 in *SMN1* was detected in 7/17 SMA patients. Deletion of exon 5 in *NAIP* gene was detected in 5/17 patients. The author concludes *SMN1* and *NAIP* gene deletions are not strange in SMA patients in Vietnam. In addition, the author emphasizes in the importance of introducing PCR and enzyme digestion to diagnose SMA in Vietnam.
Deletions in the survival motor neuron gene in Iranian patients with spinal muscular atrophy	2009`	Academic Literature	Original Article	Epidemiology Genetics	Iran	LMIC	Middle East and North Africa	English	The article estimates the frequency of exon 7 deletion in *SMN1* gene in Iranian patients with SMA symptoms, or in fetus of pregnant women with SMA relatives. 195/243 subjects were diagnosed with SMA type I, 30/243 with SMA type II and 18/243 with SMA type III. The percentage for SMA type I, II and III patients with homozygous deletion for exon 7 in *SMN1* gene were 94%, 95%, and 100%, respectively. The relate of deletion of *SMN1* exon 7 is similar to frequencies reported In China, Tunisia or Western Europe. The author highlights the importance of

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									prenatal diagnoses, and genetic counseling in a country with high proportion of consanguineous marriages.
Economic Burden of Spinal Muscular Atrophy from the Perspective of Public Health Institutions in Mexico	2022	Academic Literature	Conference Abstract	Health Technology Assessment	Mexico	UMIC	Latin America and Caribbean	English	The conference abstract calculates the economic burden of treating patients with SMA type I versus SMA type II and III. Direct medical cost was estimated based on public sources of health institutions. The costs associated with the management of patients with SMA type I were $76,593.29, while for patients with SMA type II and III were $18,340.04 per patient and per year. However, the longer life expectancy of SMA type II and III makes the financial impact broader.
Electronic Official Gazette n. 10,545	2021	Grey Literature	Government Regulatory Document	Regulation	Brazil	UMIC	Latin America and Caribbean	Portuguese	The decree no. 15.698, of 21 June 2021 decrees transaction with drugs Spinraza (Nusinersen) and Zolgensma (Onasemnogene abeparvovec) are exempt from taxes on transactions relating to the movement of goods and on the provision of interstate and intercity transport and communication services (ICMS).

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
Evaluation of quality of life of patients with rare neuromuscular diseases in a University Hospital in Rio de Janeiro/Brazil	2021	Academic Literature	Conference Abstract	Quality of Life and Comorbidities	Brazil	UMIC	Latin America and Caribbean	English	The study tried to evaluate the quality of life with patients with rare neuromuscular diseases, including SMA. The author concludes depression is a risk factor for fatigue and dysphagia.
Excluded - Living with disabilities in Yemen armed conflict	2019	Grey Literature	NGO Report	Quality of Life and Comorbidities	Yemen	LIC	Middle East and North Africa	English	The report documents testimonies of the burden faced by patients with disabilities and their families in Yemen's armed conflict. The report documents a case of a mother dealing with the stigma and the lack of resources for treating her 3 years old daughter, affected with SMA. The mother explains the health situation of her daughter went worst after leaving in a camp with scarce ventilation. She reports her daughter does not have the ability to hold up her neck, walk, sit or crawl.
Experience in the Treatment with Pyridostigmine Monotherapy, in Patients with Spinal Muscular Atrophy in Colombia	2022	Academic Literature	Conference Abstract	Treatment and Access to Care Quality of Life and Comorbidities	Colombia	UMIC	Latin America and Caribbean	English	The study studied the use of the acetylcholinesterase inhibitor pyridostigmine in SMA patients non eligible for targeted therapy approved in Colombia. Initial response and follow-up based on motor scores were documented for distal tremor, lingual fasciculations and final motor functionality. There

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									was a (positive) significant score for distal tremor and lingual fasciculations. The author concludes pyridostigmine, although not being a disease-modifying drug, can improve the quality of life of patients.
Factors associated with delayed diagnosis of spinal muscular atrophy in China and changes in diagnostic delay	2001	Academic Literature	Article	Diagnosis	China	UMIC	East Asia and Pacific	English	The article studies the factors that contributed to delays in SMA diagnosis. Between 2013 and 2018, 205 families with SMA were studied. SMA type I, II, and III patients are diagnosed in a time window of 3.38, 4.08 and 11.37 months, respectively. In addition, SMA type III patients had to visit more doctors than SMA type I and II to obtain a diagnosis (3.95 vs 2.56 doctors). Results of this study were compared to a previous cohort. Birth order, caregiver, parent's educational level and economic status, did not have an impact on diagnosis. However, those who were genetically tested in their first visit did have an early diagnosis. Children's hospitals and neurologic departments were found to detect earlier SMA. Lastly, patients who visited Chinese elite cities had a relatively shorter time window. Compared to the prior

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									cohort (2003-2008), the diagnostic time window for types II and III were 54.67 and 62.10% shorter, respectively. The author explains this difference due to the improvement in the medical capacity. In addition, the author highlights the importance of detecting the early signs of abnormal growth and development in kids by caregivers.
Frequency of SMN1 deletion carriers in a Mestizo population of central and northeastern Mexico: A pilot study	2015	Academic Literature	Article	Epidemiology	Mexico	UMIC	Latin America and Caribbean	English	The article studies the prevalence of SMA and carrier frequency of heterozygous deletion of *SMN1* gene from two mestizo populations in northeastern and central Mexico. The predicted carrier frequency was 2.62% (11/420), although this carrier frequency was higher in northeastern than in central population (3.14% vs 1.5%). No significant difference was observed between the two populations. The author concluded there were no significant differences between the Mexican populations studied and other ethnic populations such as African American, Asian, Korean, or Jewish populations. In addition, the author mentions the calculated prevalence differs from previous

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									studies performed in in Hispanic populations. A previous study found SMA carrier frequency in Hispanic American people were of 0.8% (8 in 1,030). The author highlights the term Hispanic encompass a highly genetically diverse group and suggests differences from studies can be expected.
Gene therapeutic strategies and relevant clinical trials in neuromuscular disorder in China	2020	Academic Literature	Review Article	Treatment and Access to Care	China	UMIC	East Asia and Pacific	English	The review highlights SMA is an autosomal recessive, progressive neurodegenerative disorder caused, in 95% of the patients, by deletions in *SMN1* gene. In addition, the review mentions three drugs that have been/are being developed to treat SMA: nusinersen, risdiplam, and onasemnogene abeparvovec. On April 28th, 2019, Nusinersen was approved in China. Since October 2019 up to the date the review was written, almost 50 patients have been treated with nusinersen. In April 2020, Chinese government has granted the consideration to registration risdiplam in the country. The clinical trials for onasemnogene abeparvovec were still taking place, so data in long-term safety and adverse effects is

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									still lacking. Still, treatment with nusinersen is expensive. The author calls for measures to guarantee all SMA patients are treated. Evidence suggests treatment with risdiplam supposes a more convenient administration mode. Being a small molecule, risdiplam is systemically distributed. In addition, an indirect comparison suggested an advantage of onasemnogene abeparvovec versus nusinersen in overall survival, independence from ventilation, motor function, and motor milestones. Onasemnogene abeparvovec (single dose) was also cost-effective compared for nusinersen (chronic treatment).
Gene therapy for selected neuromuscular and trinucleotide repeat disorders – An insight to subsume South Asia for multicenter clinical trials	2023	Academic Literature	Research Paper	Genetics Treatment and Access to Care	Sri Lanka	LMIC	South Asia	English	The article studies the genetic mutations in SMA patients to design treatment strategies. It also mentions consanguinity is not as common as in other South Asian countries. MLPA and single plex PCR were used to diagnose SMA. Of 66 patients suspected to have SMA, 22 patients (34%) were found to have no copy of *SMN1* gene. The number of *SMN2* gene copies varied between patients.

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									The most common subtype was SMA type 2, with 7 patients. The second most common SMA type was 3, with 6 patients, followed by SMA type 0 and 1, with 4 patients, and SMA type 4, with 1 patient. The author highlights that most clinical trials for SMA are being performed in the HIC, and no clinical trial was performed in South Asia. According to the results of the study, only 23% of patients in Sri Lanka with SMA are eligible to gene therapy. This is aligned with previous data from South India (31% of patients eligible) and from Pakistan (22%). The author concludes there is a lack of knowledge on efficacy and safety of targeted therapies in countries in South Asia.
Genetic profile of spino-muscular atrophy and its clinical correlation in a tertiary care centre: A study from Eastern India	2019	Academic Literature	Conference Abstract	Genetics Epidemiology Diagnosis Quality of Life and Comorbidities	India	LMIC	South Asia	English	The study aimed to estimate the mutation rate in *SMN1* gene in SMA patients from Eastern India. Only patients with clinically and genetically confirmed SMA were included in the study. Of 25 patients included, 40% were diagnosed with SMA type I. Deletion of both exons 7 and 8 was the most common deletion. There was a delayed diagnosis for 21 of

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									25 patients. Hypotonia was the most common symptom.
Genetic testing for spinal muscular atrophy (SMA) in South Africa	2006	Academic Literature	Scientific Letter	Genetics	South Africa	UMIC	Sub Saharan Africa	English	The letter points that white South African SMA patients have clinical presentation and genetics similar to that of most European countries. In contrast, SMA in the black community differed. A previous study showed that homozygous *SMN1* deletion was more common in white SA SMA patients (90-95%) than in black SA SMA patients (65%). Another study reduced this percentage even lower, to 51%. Additionally, of the non-deletion SMA patients, at least 70% had a heterozygous deletion for *SMN1* gene, suggesting a SMA diagnosis. It is hypothesized that a second mutation, together with the heterozygous deletion of *SMN1* gene, could be the cause of the disease. Author points out the need to elucidate the molecular causes of SMA in black SMA patients.
Genetic Testing in Emerging Economies (GenTEE)	2013	Grey Literature	European Commission Summary Report	Diagnosis Epidemiology	India South Africa	LMIC UMIC	South Asia Sub Saharan Africa	English	GenTEE project reports the advance in genetic services in 8 emerging economies: Argentina, Brazil, China, Egypt, India, Oman, Philippines, and South Africa. The

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									report mentions India has an estimated SMA prevalence of 0.1 per 1,000 births, accounting to 2,700 births in 2010. Thereby, SMA is one of the most common single gene disorders in India. Molecular genetic testing is available for SMA in India. In South Africa, SMA prevalence among black South African population is of 1/2.,000. In addition, the report highlights that in the tertiary health care sector there is carrier screening for several recessive disorders, including SMA.
Health system and the appraisal of medicines for rare diseases in England and Brazil: A comparative analysis	2020	Academic Literature	Conference Abstract	Health Technology Assessment	Brazil	UMIC	Latin America and Caribbean	English	The study aimed to compare CONITEC (Brazil) and NICE (UK) recommendation reports for medicines targeting rare diseases. Nusinersen and other medicines were assessed. Neither CONITEC nor NICE contemplated all domains proposed by European HTA network (EUnetHTA). Decision making was not only based on technical and scientific aspects, but value judgments too. Uncertainties arose in several aspects: clinical, cost-effectiveness, well-being benefits, budget impact, and social pressure. The author concludes

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									new mechanisms to evaluate medicines targeting rare diseases need to be developed.
Health-related quality of life in Thai children with spinal muscular atrophy	2022	Academic Literature	Original Article	Quality of Life and Comorbidities Patient, Family and Public Perspectives	Thailand	UMIC	East Asia and Pacific	English	The study tried to evaluate the health-related quality of life (HRQoL) of the pediatric population in Thailand. HRQoL was measured using the Thai version of the Pediatric Quality of Life Inventory™ 4.0 Generic Core Scale (PedsQL™). PedsQL™ was significantly lower in SMA Thai patients (57.3 ± 13.6) and their parents (54.3 ± 14.8) than in healthy Thai children (78.7 ± 9.3) and their parents (79.0 ± 12.8). Physical health scores of SMA patients were lower than in healthy individuals (32.7 vs 82.1). This difference between SMA and healthy individuals was less pronounced for psychosocial health (70.8 vs 77.0). When comparing the SMA types, the highest PedsQL™ were for SMA type III patients and the lowest for type I. In addition, there was moderate to good correlation between SMA patients and parents' self-reports. Non-ambulation, lower household income, mechanical ventilation,

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									and inability to attend school were associated with lower HRQoL. The author highlights Thai SMA patients do not receive the same level of support than in other countries. Devices designed to help SMA patients are not covered by Thai universal health care insurance. Thereby, contributing to a lower quality of life.
High incidence of SMN1 Exon 8/9 deletions in spinal muscular atrophy (SMA)	2021	Academic Literature	Conference Abstract	Genetics Epidemiology	India	LMIC	South Asia	English	The study aimed to estimate the frequency of SMA patients lacking exons 7 and 8 from *SMN1* gene in South India. Individuals with SMA symptoms or having family history of SMA were included. Of 60 patients, 27 (45%) had a homozygous deletion in exons 7 and 8, and 23 (38%) were carriers for either exon 7 or 8 deletions. All patients with SMA symptomatology had a homozygous deletion in *SMN1* exons 7 and 8. The author pointed out the incidence of exons 7 and 8 in *SMN1* was high.
Incidence of spinal muscular atrophy in Armenia: 2012-2018	2019	Academic Literature	Conference Abstract	Epidemiology	Armenia	UMIC	Europe and Central Asia	English	The study aimed to describe the epidemiology of SMA in Armenia. The study included all subjected patients between 2012 and 2018 that underwent a genetic test. Of

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									99 patients, 37 (37.4%) were confirmed by genetic testing to have SMA. Of 12 prenatal testing, SMA was confirmed in 2 cases. In both cases the pregnancy was terminated. Of the patients diagnosed with SMA, 59.5% were diagnosed with SMA type I, 27 with SMA type II, and 10.8% with SMA type III. The estimated SMA incidence in Armenia is 13.2 in 100,000. This incidence is similar to the observed in Eastern Europe.
Living with Disability in Mongolia: Progress Toward Inclusion	2019	Grey Literature	Organization Report	Quality of Life and Comorbidities	Mongolia	LMIC	East Asia and Pacific	English	The report mentions the concept of medical and labor accreditation commissions (MLACs). MLAC disability assessments decide on disability based on diagnosis and provide a disability range for different diseases. This range for SMA is 70-100%, what makes SMA patients eligible for a full disability pension. If the person does not have a work history and doesn't quality for a disability pension, MLAC can provide a social welfare pension.
Managed Entry Agreements in the Context of Health Technology Assessment Recommendations in	2022	Academic Literature	Conference Abstract	Health Technology Assessment	Ukraine	LMIC	Europe and Central Asia	English	The study aimed to review Managed Entry Agreements (MEAs) implementation in the Ukrainian HTA environment. All

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
Ukraine: Analysis on the Stage of Development									Ukrainian legislative acts concerning MEAs and HTA were included and analyzed. The Minister of Health had addressed applicants to negotiate a MEA for 5 medicines, including risdiplam. The author concludes legislative acts for MEAs and HTA tries to improve patient's access to innovative medicines.
Management of neuromuscular diseases and spinal muscular atrophy in Latin America	2017	Academic Literature	Review	Treatment and Access to Care	Brazil Mexico Venezuela Colombia Paraguay Peru El Salvador Honduras Nicaragua Guatemala	UMIC UMIC Not-classified UMIC UMIC UMIC LMIC LMIC LMIC UMIC	Latin America and Caribbean	English	The review describes the management and care of neuromuscular diseases, including SMA, in Latin America. Due to economic, cultural, political and health care differences, care of SMA patients varied across Latin America. Several clinical studies of Latin American SMA patients had been published in the last decades. Gene characterization, molecular and carrier status studies had been performed in Brazil since 2003-2011. Other countries, such as Mexico were growing translation research abilities on SMA. Parent organizations for SMA had been created in countries like Brazil, Mexico, or Venezuela. These parents' organizations had been advocating and sponsoring

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									diagnosis, care, and research. In addition, local registries of SMA patients were present on Mexico, and was being developed in Brazil. Televised fundraising events for kids with disabilities, are present in several Latin American Countries: El Salvador, Peru, Mexico, Honduras, Nicaragua, Guatemala, Paraguay, and Colombia. Around 230,000 children, including SMA patients, have benefited from this program. However, in many Latin American countries there was still no care for SMA patients. The author pointed out the need for more awareness and efforts to expand national registries for SMA.
Managing intrathecal administration of nusinersen in adolescents and adults with 5q-spinal muscular atrophy and previous spinal surgery	2020	Academic Literature	Article	Treatment and Access to Care	Brazil	UMIC	Latin America and Caribbean	English	The article studied the use of imaging-guided intervention for the intrathecal administration of nusinersen in SMA patients. Intrathecal administration requires four lumbar punctures during two months-period and consecutive maintenance injections every four months. The study analyzed nusinersen injection in SMA patients with posterior thoraco-lumbar spinal fusion. The author concludes imaging-guided

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									intervention is needed in patients with previous spinal surgery. In addition, the authors mention injections should be guided by CT or fluoroscopy.
Managing pregnancy in a spinal muscular atrophy type III patient in Indonesia: a case report	2020	Academic Literature	Case Report	Genetics Treatment and Access to Care	Indonesia	LMIC	East Asia and Pacific	English	The case report showed the case of a pregnant woman who started to show SMA symptoms at the age of 8, although she showed delayed development before 26 months old. In her second pregnancy, both her and her first daughter underwent SMA genetic testing. Genetics results confirmed that the mother was SMA patients and her daughter a carrier. She was provided genetic counseling and decided to continue the pregnancy. Neither Nusinersen nor gene replacement therapy were available in Indonesia. In addition, the author highlights genetic testing is not covered by the national health insurance. The current study adds to previous case reports performed in Indonesia.
Medicinal Products Regulation in Brazil	2018	Grey Literature	Government Report	Regulation	Brazil	UMIC	Latin America and Caribbean	English	The report provides an insight into the medicinal product regulations in Brazil. It introduces RDC 205/2017 – Special procedure for

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									rare diseases. This procedure guarantees flexibility in technical requests and encourages submission in different regions. It has been used for new treatments for SMA.
MLPA based SMN1 deletion analysis: Clinical correlation in Indian patients with Spinal Muscular Atrophy	2018	Academic Literature	Conference Abstract	Genetics Epidemiology	India	LMIC	South Asia	English	The study aimed to test MLPA in the SMA diagnosis and to correlate genetic diagnosis with clinical characteristics. Genetically confirmed SMA patients who attended a quaternary care center for neurological disorders in India between 2012 and 2018 were included. In total, 96 patients were diagnosed with SMA. Of them, 39 (60.6%) were diagnosed with SMA type I, 21 (22%) with type II, 14 (14.6%) with type IIIA, 19 (19.8%) with type IIIB, and 3 patients (3.1%) with type IV. Consanguinity was present in 28 families, and 8 patients had also affected siblings. Tongue fasciculation was the most common feature in SMA patients type I, II and IIIA, and calf hypertrophy in patients type IIIB and IV. Of all patients, 74 (77%) had combined *SMN1* deletions in exons 7 and 8, and isolated exon 7 deletions in 24 patients (25%). Between patients with SMA type

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									III, those with an isolated exon 7 deletion had the milder form of the subtype, IIIB. Isolated exon 8 deletions were not present. The author suggested that exon 8 deletion was not a cause of SMA.
Molecular analysis and prenatal prediction of spinal muscular atrophy in Chinese patients by the combination of restriction fragment length polymorphism analysis, denaturing high-performance liquid chromatography, and linkage analysis	2007	Academic Literature	Original Contribution	Genetics Epidemiology Diagnosis	China	UMIC	East Asia and Pacific	English	The study aimed to optimize SMA prenatal screening. 77 Chinese families were included in the study. 87 SMA patients, and 132 parents were screened for their SMA status. In addition, prenatal screening was performed on 11 fetuses from 10 families. Of 77 families, 72 (93.5%) had a deletion in *SMN1* gene, 1 had a deletion in *SMN2* gene, and 4 had no deletion. Results were based on RFLP analysis and DHPLC. Of the 5 patients without the *SMN1* deletion, 2 had two copies of the *SMN1* gene, and 3 had only one copy. Of 11 fetuses tested, 4 were found to have the *SMN1* deletion and were aborted. Of the 7 healthy fetuses, 4 fetuses and all of the 14 parents were carriers. The author suggested a diagnosis system to identify SMA patients and their families. The system consisted of: RFLP analysis and DHPLC to detect *SMN1* deletion, *SMN1* copy

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									number quantification, SMN coding region sequencing for patients only having 1 *SMN1* copy, and if patients had a subtle mutation, reverse-transcriptase-PCR to discover whether the mutation is present on *SMN1* or *SMN2* gene. The author pointed out DHPLC to have superiority over other SMA carrier tests.
Molecular analysis of the SMN and NAIP genes in Iranian spinal muscular atrophy patients	2009	Academic Literature	Original Article	Genetics Epidemiology	Iran	LMIC	Middle East and North Africa	English	The study aimed to determine the frequency of *SMN* and *NAIP* gene deletions in SMA patients from Iran. Of the SMA patients included, 54 were type I, 8 type II, and 13 type III. Of the 75 SMA patients, 68 (90%) showed a homozygous deletion of exons 7 and 8 in *SMN1* gene. SMN deletions were found in 49/54 (91%) SMA type I patients, in 7/8 (87%) type II patients, and 12/13 (92%) type III patients. This is similar to other studies from other countries like China, Germany, Japan, Spain, Singapore, or United States. Of the 68 patients with deletions, 63 (92.6%) had deletions of both exon 7 and 8, 4 (5.9%) only in exon 7, and 1 (1.5%) only in exon 8. Deletion of exon 5 of *NAIP* gene was associated with disease

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									severity. *NAIP* deletion was found in 40/54 (74%) of patients with type I, in 2/8 (25%) of type II and in 1/13 (7.7%) of type III. All patients with *NAIP* deletion had deletions in *SMN* gene.
Molecular analysis of the SMN1 and NAIP genes in Iranian patients with spinal muscular atrophy	2007	Academic Literature	Original Article	Genetics Epidemiology	Iran	LMIC	Middle East and North Africa	English	The study aimed to genetically characterize the childhood onset of SMA in Iranian patients. Of 75 patients with a clinical diagnosis, 73 (97%) had a homozygous deletion in exon 7 and 8. Homozygous deletions in both exons were found in 100% patients with SMA type I, 66% with type II, and 50% with type III. In addition, 62 (83%) had a homozygous deletion in exon 5 and 6 in *NAIP* gene. Homozygous deletions in both exons were found in 87% of patients with SMA type I, and 33% for patients with type II. Deletions in both *SMN1* and *NAIP* genes were found in 87% of patients with SMA type I, in 33% of patients with SMA type II, and in no patient with SMA type I. Parallelly, 251 samples from chorion callus sampling from, parents, siblings and control individuals were tested. Homozygous deletions of *SMN1* and *NAIP* genes in the CVS

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									were 21% and 71%, respectively. The rate of consanguineous marriages in the families studied was 97%.
Molecular characterization of SMN copy number derived from carrier screening and from core families with SMA in a Chinese population	2010	Academic Literature	Article	Genetics Epidemiology	China	UMIC	East Asia and Pacific	English	The study aimed to determine the copy number of *SMN* genes in 1712 newborn cord blood samples in southern China and 25 SMA families (26 SMA patients and 44 parents) to identify carriers. Of 1712 newborns, 1535 subjects had 2 copies of *SMN1* gene, 119 had 3 copies, 17 had 4 copies, and 41 had a heterozygous deletion of *SMN1* exon 7. Thereby, carrier frequency was established at 1/42 (2.39%) in Chinese population. In addition, duplicated *SMN1* alleles and de novo mutations were rare in SMA carriers. Of the 26 SMA patients, 13 cases were diagnosed with SMA type I, 5 with type II, and 8 with type III. 24 patients had a homozygous deletion of *SMN1* gene, and 2 had a heterozygous deletion. Of 44 parents, 40 (90.9%) had the 1+0 genotype, 2 had the 2+0 genotype, and 2 had 1+1 D' genotype.
Molecular genetic study of Spinal Muscular Atrophy in Southern India	2005	Academic Literature	Conference Abstract	Genetics Epidemiology	India	LMIC	South Asia	English	The study aimed to identify deletions in the *SMN1* and *NAIP* genes for 51 patients. In SMA type I patients, 42% had deletions in both *SMN1* and *NAIP* genes. In

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									SMA type II patients, 80% had deletions in the *SMN1* gene. Deletions occurred in half of the patients. The author highlighted the differences between India, with a relative low percentage of deletions (50%) compared to the worldwide SMA population (96%).
Mutation analysis of 419 family and prenatal diagnosis of 339 cases of spinal muscular atrophy in China	2020	Academic Literature	Research Article	Genetics Epidemiology	China	UMIC	East Asia and Pacific	English	The study aimed to genetically characterized 419 SMA patients and 330 fetuses in China. Of 419 SMA patients, 404 (96.4%) had a deletion of exon 7 in *SMN1* gene. Of these, 168 (42%) were diagnosed with SMA type I, 121 (30%), with type II, 99 with type III (24%), and 16 (4%) with type IV. Of the 419 cases, 15 (3.6%) had a heterozygous deletion of *SMN1* with a point mutation. Of 419 patients, 11,46% of patients had one copy of *SMN2* gene, 65.87% had two copies, 19,57% had three copies, and 3,10% had four copies. In addition, of the 339 prenatal diagnosis, 72 SMA cases and 267 carriers were reported.
NGS-based spinal muscular atrophy carrier screening of 10,585 diverse couples in China: a pan-ethnic study	2020	Academic Literature	Article	Genetics Epidemiology	China	UMIC	East Asia and Pacific	English	The study aimed to perform SMA carrier screening in 10,585 couples (21,170 individuals) in South China. In total, 20,883

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									samples were included in the analysis after discarding samples with low quality. Carrier frequency was estimated to be 1 in 73.8 (1.4%), although there were differences between ethnic groups. Dai ethnicity showed the lowest carrier frequency (0%), and Tujia the highest (4,3). Yao (3.5%) and Yi (2.5%) ethnic groups also showed significantly high carrier frequencies in comparison with overall population. There were not significant differences between the provinces included (Guangdong, Guangxi, Hainan, Yunnan, and Guizhou). Of the 283 carriers detected, 236 (83.4%) had more than one copy of *SMN2* gene.
Official Gazette n. 9,658	2018	Grey Literature	Government Regulatory Document	Regulation	Brazil	UMIC	Latin America and Caribbean	Portuguese	The city hall of Campo Grande in Brazil notifies the company Panamby Medicamentos e Seviços LTDA about the procurement process related with the acquisition of the medicine Nusinersen. The city hall intends to cancel the dispensation of nusinersen according to article 4949, § 3º da Lei 8.666/93.

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Prenatal or preconception carrier screening for spinal muscular atrophy in Wuhan City of China	2020	Academic Literature	Conference Abstract	Epidemiology Genetics Diagnosis	China	UMIC	East Asia and Pacific	English	The study aimed to estimate the carrier rate in Wuhan City, in China. Carrier frequency was estimated to be 1 in 58 (1.7%) in women. Of the 52 women, 47 (90.4%) of their spouses received carrier screening. Among the 52 spouses, 7 (13.4%) were determined to be SMA carriers. Invasive amniocentesis was performed in three pregnant women, and SMA was diagnosed in one fetus.
Prevalence of genetic disorders in the northwest of Iran	2010	Academic Literature	Conference Abstract	Genetics Epidemiology	Iran	LMIC	Middle East and North Africa	English	The study aimed to estimate the prevalence of different genetic disorders in Iran. SMA was the third most common genetic disorder, after familial Mediterranean fever and inherited deafness, with 11.1 cases per 100,000 population (CI 95% 10.1-12.1).
Progression of the Revised Hammersmith Scale Items in Patients with Spinal Muscular Atrophy Treated with Nusinersen	2022	Academic Literature	Conference Abstract	Quality of Life and Comorbidities Patient, Family and Public Perspectives	Colombia	UMIC	Latin America and Caribbean	English	The study aimed to assess the impact of treatment with nusinersen on quality of life in SMA patients and their caregivers. 23 SMA patients were included. Of them, 19 were diagnosed with SMA type II and 4 with SMA type III. Their caregivers were included

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									as well. Psychosocial health score improved, both self-reported and proxy reported. No significant difference was observed in the physical health score. In addition, patient responsibility and financial burden increased. Self-reported score on PedsQL GCS correlated with Hammersmith Functional Motor Scale – Expanded.
Quality of life of children with spinal muscular atrophy and their caregivers from the perspective of caregivers: a Chinese cross-sectional study	2021	Academic Literature	Research Article	Quality of Life and Comorbidities Patient, Family and Public Perspectives	China	UMIC	East Asia and Pacific	English	The study aimed to evaluate the quality of life of SMA patients and families in China. Children with SMA type III scored better on neuromuscular disease and family resources PedSQL parameters than SMA type I and type II patients. In addition, caregivers of patients with SMA type I reported higher scores in physical, emotional, social, and cognitive domains in comparison with children with types I and II. Limited mobility, skeleton deformity, stable course of disease, respiratory support and digestive system dysfunction were associated with lower scores. Exercise, multidisciplinary team management and use of Nusinersen were associated with higher scores. The author

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									concluded the article mentioning the importance of multidisciplinary team to improve quality of life.
Resolution 205 of 2020	2020	Grey Literature	Government Policy Document	Policy	Colombia	UMIC	Latin America and Caribbean	Spanish	Nusinersen is not included in the health services and technologies financed from the maximum budget.
Restrictions in use and availability of pharmaceuticals, 2010-2018	2020	Grey Literature	WHO Report	Treatment and Access to Care	Brazil	UMIC	Latin America and Caribbean	English	The report documents health professionals in Brazil were informed of hydrocephalus related to bleeding or meningitis in SMA patients treated with nusinersen. Physicians were advised to discuss potential risks to SMA patients and caregivers, as well as to assess hydrocephalus in patients with associated symptomatology.
Results 2017 - Agência Nacional de Vigilância Sanitária - Anvisa	2017	Grey Literature	Health Authority Report	Treatment and Access to Care	Brazil	UMIC	Latin America and Caribbean	English	The report documents nusinersen to become a therapeutic option in Brazil, after gaining registration.
Risdiplam: First Approval	2020	Academic Literature	Insight Report	Treatment and Access to Care	Brazil China Indonesia	UMIC UMIC	Latin America and Caribbean East Asia and Pacific	English	The report focusses on the medicine risdiplam for the treatment of SMA. The author emphasized risdiplam makes gene *SMN2* to produce full-length and functional *SMN1* protein. At the time of the report, risdiplam was in the pre-registration phase in

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									several countries, such as Brazil, China, or Indonesia.
Screening of SMA carrier status in Republic of Moldova	2020	Academic Literature	Conference Abstract	Genetics Epidemiology	Moldova	UMIC	Europe and Central Asia	English	The study aimed to screen for SMA carriers 15 couples (30 persons). Of 30 subjects, 22 (73%) had two copies of *SMN1* gene, and 8 (26%) had a heterozygous deletion in *SMN1* gene. In one couple, both subjects were heterozygous for the deletion.
SMA carrier testing using Real-time PCR as a potential preconception screening tool	2022	Academic Literature	Research Article	Genetics Epidemiology Treatment and Access to Care	Egypt	LMIC	Middle East and North Africa	English	The study aimed to use quantitative real-time PCR to determine the copy number of *SMN1* gene in Egypt. 115 healthy individuals (including 53 married couples) and 10 SMA families were included in the study. Of the 53 married couples, in 33 families (66 subjects) both parents were carriers. 6 families underwent prenatal diagnosis, and diagnoses were confirmed for 2 fetuses. In 16 families, one parent was a carrier and the other was not. In 3 families, no carrier was detected. Of all studied subjects, 75.7% of them were carriers, accounting to a high estimated carrier frequency. The author also mentioned how important is the SMA carrier screening program due to the high

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									rate of consanguinity in Egypt. The Egyptian National Drug Authority approved the use of risdiplam in June 2021.
SMN genes molecular testing in a cohort of 1546 subjects tested for genetic diagnosis and trial enrollment	2019	Academic Literature	Conference Abstract	Genetics Epidemiology	North Africa West Africa Pakistan	None None LMIC	Middle East and North Africa Sub Saharan Africa South Asia	English	The study aimed to calculate the frequency of different *SMN1* genotypes in 1546 subjects (including 60 prenatal tests). Of all subjects, 4.6% had a homozygous deletion, 16% a heterozygous deletion, and 6.5% a heterozygous duplication (three copies). Most patients with duplication of *SMN1* gene were from North and West Africa and Pakistan.
Spinal muscular atrophy	2019	Academic Literature	Conference Abstract	Epidemiology Genetics	Tunisia	LMIC	Middle East and North Africa	English	The author pointed out how the high frequency of consanguinity in Tunisia seems to be associated with a higher prevalence of SMA. The retrospective study included 70 patients that were referred as SMA patients between 1992 and 2019. Of all patients, 33 were genetically tested for the deletion of exons 7 and 8 in *SMN1* gene, and exons 5 and 13 in *NAIP* gene. After neurological evaluation, myopathic syndrome was observed in all patients, osteotendinous areflexia in 55 (78.6%), fasciculations in 15

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									(21.5%). Atrophy and muscle weakness were the most common clinical symptoms. Respiratory and bulbar muscle impairment was observed in the latest stages of the disease, especially in SMA type I. Consanguinity was present in 55.71% of the families. In the 33 patients genetically tested, 15 (45.4%) had a homozygous deletion in *SMN1* gene, and 3 (9.1%) in *NAIP* gene. Deletions in *NAIP* gene were associated with most severe forms of the diseases.
Spinal muscular atrophy carrier frequency and estimated prevalence of the disease in Moroccan newborns	2012	Academic Literature	Short Report	Epidemiology	Morocco	LMIC	Middle East and North Africa	English	The study aimed to calculate the carrier frequency of exon 7 deletion in *SMN1* gene and the SMA prevalence in Morocco. Reliable quantitative al-time polymerase chain reaction assay with SYBR Green I dye was used to determine the copy number of *SMN1* gene in 150 Moroccan newborns. Carrier frequency was estimated to be 1 in 25 cases (4%). After considering high degree of consanguinity in Moroccan population and that 95% of SMA patients are homozygous for *SMN1* deletion, SMA prevalence was estimated to be 1 in 1,800. This prevalence was higher than in

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									European countries, but similar to Middle Eastern countries. The author pointed out the importance of genetic carrier testing for families with SMA history.
Spinal muscular atrophy carrier frequency in Ukraine	2013	Academic Literature	Short Communication	Epidemiology	Ukraine	LMIC	Europe and Central Asia	English	The study aimed to estimate the SMA prevalence in Ukraine. 370 healthy Ukrainian subjects were included in the study. Carrier frequency was estimated to be 1 in 31 (3.24%). The authors highlighted this carrier frequency is high in comparison with other Caucasian peoples, although they mentioned this could be explained due to the small Ukrainian sample.
Spinal Muscular Atrophy in the Black South African Population: A Matter of Rearrangement?	2020	Academic Literature	Original Research Article	Epidemiology Genetics	South Africa	UMIC	Sub Saharan Africa	English	The aim of the study was to elucidate the genetic cause of SMA in the black South African population. MLPA testing was performed on 197 black patients. Of them, 75 had a homozygous deletion of exon 7 in *SMN1*, 50 had a homozygous deletion of exon 7 in *SMN2*, and 72 patients did not have any homozygous deletions. Of the 72 patients with no homozygous deletions, only 6 (8.3%) had heterozygous deletions of exon 7 in *SMN1* gene. This result was lower than in

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									previous studies. Furthermore, 38 white SMA patients (30 and 8 with homozygous deletion of exon 7 in *SMN1* and *SMN2* genes, respectively. 122 black and 30 white negative controls were included as well. Of 122 black negative controls, 62 (50.8%) had more than two copies of exon 7 in *SMN1* gene. These results coincide with was observed in previous research performed in black Sub-Saharan Africa, and black African American population. Of 30 white controls, only 1 (3.3%) had more than two copies of exon 7 in *SMN1* gene. The same effect was observed for exon 8 in *SMN1* and exon 5 in *NAIP* gene. For the black SA control, 67 (54.9%) and 46 (37.7%) had multiples copies of exon 8 in *SMN1* gene and exon 5 in *NAIP* gene, respectively. For the white SA control, the values decreased to 2 (6.7%) and 4 (13.3%), respectively. There were no significant differences in the copy number of exon 7 in *SMN2* gene between white and black controls, but there were in the copy number of exon 7: 33 (27%) in black, and 2 (6.7%) in white. In addition, the copy number of exons

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									7, 8 in *SMN1* gene and exon 5 in *NAIP* gene ranged from 1 to 6 in black SA controls, in contrast to white SA controls. In addition, for SA SMA patients who had a homozygous deletion of exon 7 in *SMN1* gene, there were significant differences between black and white subjects in the copy number of exon 8 in *SMN1* gene, of exon 7 in *SMN2* gene, and exon 5 in *NAIP* gene. The author highlighted MLPA not to be an appropriate technique for detecting SMA carriers in South African black population. In addition, SA SMA patients with a homozygous deletion of exon 7 in *SMN1* showed more frequently large deletions in other regions in *SMN1* gene, as well as in neighboring genes. Homozygous deletion in *SMN2* gene was also widely extended in black SA population. The author concludes there is a lack of understand of the genetic causes underlying SMA in the black SA population.
Spinal muscular atrophy in Venezuela: quantitative analysis of SMN1 and SMN2 genes	2020	Academic Literature	Research Article	Epidemiology Genetics	Venezuela	Not classified	Latin America and Caribbean	English	The study aimed to investigate the number of copies of *SMN1* and *SMN2* genes in both 49 healthy subjects and 94 suspected SMA

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									patients from 29 families. The carrier frequency of *SMN1* and *SMN2* genes deletion was 0.01 (1 in 49) and 0.163 (27 in 40), respectively. Of 49 subjects, 37 (75.5%) had two copies of *SMN1* gene, 2 (4.1%) had three, 2 (4.1%), had four or five, and 1 (2%) had six copies. In 15 of 29 families with suspected SMA, it was observed a deletion of exon 7 in *SMN1* gene.
Spinal Muscular Atrophy Therapeutics in India: Parental Hopes and Despair!	2021	Academic Literature	Commentary	Treatment and Access to Care	India	LMIC	South Asia	English	At the moment of the commentary, the only treatment to SMA was supportive care (assisted ventilation, feeding, physiotherapy, orthotics, and spine stabilization). Drug Controller General of India (DCGI) granted marketing approval to risdiplam in India. In addition, nusinersen was available in the country through Individual Patient Humanitarian Access Program to selected children with SMA. Similarly, the managed access program for onasemnogene abeparvovec was open for infants and children over 2 years in countries where was not yet approved. Roche had also initiated a compassionate use program to offer risdiplam for a few

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									cases globally. The author mentioned most patients did not receive treatment. The author also mentioned that in some cases, patients with SMA type I died before finishing the documents to import the drug were ready. The author concludes mentioning alternatives to grant access to medicines: manufacturing license agreements, grant compulsory licenses, or entrance of these drugs into the insurance cover.
Spinal muscular atrophy: A frequent cause of congenital hypotonia in Morocco	2011	Academic Literature	Original Memory	Genetics	Morocco	LMIC	Middle East and North Africa	French	The study aimed to estimate the prevalence of the deletion of exon 7 in *SMN1* gene in 87 patients with an unknown cause of congenital hypotonia. Of 87 patients, 23 (38%) had a homozygous deletion of exon 7.
The First Managed Entry Agreements Based on Health Technology Assessment Approved in Ukraine: Analysis and Future Perspectives	2023	Academic Literature	Conference Abstract	Treatment and Access to Care Health Technology Assessment	Ukraine	LMIC	Europe and Central Asia	English	The conference abstract aimed to review managed entry agreement (MEA) based on HTA in Ukraine. Minister of Health included 10 MEAs at the end of 2022, including for risdiplam. Risdiplam was determined to be procured centrally for the treatment of children with SMA. The author concludes MEAs based on HTA

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									improves patients' access to innovative medicines.
The incorporation of nusinersen by the Brazilian Unified National Health System: critical thoughts on the institutionalization of health technology assessment in Brazil	2019	Academic Literature	Article	Treatment and Access to Care Health Technology Assessment	Brazil	UMIC	Latin America and Caribbean	Portuguese	The article discusses the incorporation of nusinersen in the Brazilian Unified National Health System (SUS). CONITEC is the regulatory organization that asses the incorporation of technologies in the SUS since law No. 12,410/2011. Following, Anvisa;s CMED assesses the efficacy, safety, cost-effectiveness, and budget impact of medicines. Nusinersen was registered in Brazil in August 2017, for pediatric and adult SMA patients. Federal Government spent R$ 143M on nusinersen during 2018 and until April 28, 2019. As of 2019, maximum government sale price (PMVG) of nusinersen with ICMS of 0% was R$ 247,399.94. PMVG value without taxes was R$ 220,982.77. In addition, the article highlights that two submissions were made for the drug nusinersen, one in January 2018 (rejected due to lack of evidence), and another one in January 2019 (accepted). The second submission did not have any restriction based on age nor SMA

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									subtype. Finally, in April 2019, nusinersen was incorporated for the treatment of SMA patients. Nusinersen is incorporated through a risk-sharing purchasing modality.
The natural history of infant spinal muscular atrophy in China: A study of 237 patients	2011	Academic Literature	Original Article	Epidemiology Quality of Life and Comorbidities	China	UMIC	East Asia and Pacific	English	The aim of the article was to study the natural history of 237 SMA patients in China. Of 237 SMA patients, 107 (45.1%) had SMA type I, 105 (44.4%) had type II, and 25 (10.5%) had type III. Age of onset was 3.1 ± 2.7, 8.7 ± 3.8, and 21.1 ± 11.7 months for SMA type I, II, and III, respectively. In addition, for SMA patients type I, survival probabilities at year 1, 3 and 5 years were 44.9%, 38.1%, and 29.3%, respectively. For SMA patients type II, survival probabilities were 100%, 100% and 97%, respectively. For SMA patients type III, survival probability was 100% at any interval. There were not differences on survival probability between male and female groups. Of 105 SMA patients type II, 12 (11.4%) lost the ability to sit, and of 25 patients type III, 5 (20%) lost the ability to walk. In addition, 61.5% of patients with SMA type I,

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									24.7% with SMA type II, and 30.3% with SMA type III were hospitalized due to pneumonia. 45.7% of patients with SMA type I, 15.6% with type II, and 0% with type I had incidences of feeding or swallowing. 31.0% of patients with type I, 58.9% with type II, and 41.0% with type III, had incidences of kyphoscoliosis. The author concludes mentioning survival status of type I patients in China appears to be better than in white SMA patients.
The prevalence of spinal muscular atrophy carrier in China: Evidences from epidemiological surveys	2020	Academic Literature	Systematic Review and Meta-Analysis	Epidemiology	China	UMIC	East Asia and Pacific	English	The aim of the systematic review and meta-analysis was to reliably estimate the SMA carrier frequency in China. With a total of 10 studies, the overall carrier frequency for SMA was estimated at 2% (95% CI 1.7-2.3%). The author also mentioned there was a gradual rise trend in SMA carrier frequency.
The quality of life in children with spinal muscular atrophy: a case–control study	2022	Academic Literature	Research Article	Quality of Life and Comorbidities	Iran	LMIC	Middle East and North Africa	English	The study aimed to study the health-related quality of life (HRQoL) of SMA patients in comparison to healthy subjects in Iran. The quality of health was lower in SMA patients in comparison with healthy subjects.

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									However, there was no significant difference in quality of life between patients affected with SMA type II and type III. SMA patients with mood disorders and with mothers with less than 12 years of education had lower scores in physical and psychosocial well-being. The low education of fathers was also associated with lower scores in all scales, but the physical.
Ultraexpensive gene therapies, industry interests and the right to health: The case of onasemnogene abeparvovec in Brazil	2022	Academic Literature	Commentary	Treatment and Access to Care Health Technology Assessment	Brazil	UMIC	Latin America and Caribbean	English	In Brazil, onasemnogene abeparvovec was approved by Anvisa (Brazilian Health Regulatory Agency) in August 2020. In the absence of evidence that would support onasemnogene abeparvovec's added therapeutic value over alternative treatments, the Brazilian drug pricing authority, CMED, approved in December 2020, a maximum price that was 77% lower than the price set by the manufacturer, Novartis. Then, Novartis decided not to commercialize the treatment in Brazil. Onasemnogene abeparvovec was not available in Brazil at the date of January 2022. Thereafter, families sued the government, in base of their right

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
									to health, to have access to onasemnogene abeparvovec. Courts have obliged Ministry of Health to fund the treatment at prices more than three times higher than the maximum approved price.
Utility estimations of different health states of patients with type I, II, and III spinal muscular atrophy in China: A mixed approach study with patient and proxy-reported data	2022	Academic Literature	Original Research Article	Quality of Life and Comorbidities	China	UMIC	East Asia and Pacific	English	The study aimed to evaluate health-related quality of life in SMA patients using health state utility values (HSUV). The author concluded that the better health states, the higher were the HSUV values. In addition, there were not statistically differences between the different SMA types.
WHO Drug Information 2017, vol. 31, 2	2017	Grey Literature	WHO Report	Treatment and Access to Care	Global	None	Global	English	The report provides the Anatomical Therapeutic Chemical (ATC) classification for several medicines, including nusinersen. ATC for nusinersen is M09AX07.
WHO Drug Information 2017, vol. 31, 4	2017	Grey Literature	WHO Report	Treatment and Access to Care	Global	None	Global	English	The report provides the Anatomical Therapeutic Chemical (ATC) classification, Defined Daily Dose (DDD) and administration route for several medicines, including nusinersen. Nusinersen ATC and DDD are M09AX07 and 0.1mg, respectively. Nusinersen is administrated parenterally.

Record	Year	Type	Subtype	Topic	Country(s)	Classification	Geographic region(s)	Language	Summary
WHO Drug Information 2019, vol. 33, 4	2019	Grey Literature	WHO Report	Treatment and Access to Care	Global	None	Global	English	The report provides the Anatomical Therapeutic Chemical (ATC) classification for several medicines, including onasemnogene abeparvovec and risdiplam. ATC code for onasemnogene abeparvovec and risdiplam are M09AX09 and M09AX10.
WHO Drug Information 2021, vol. 35, 4	2020	Grey Literature	WHO Report	Treatment and Access to Care	Global	None	Global	English	The report provides the Anatomical Therapeutic Chemical (ATC) classification, Defined Daily Dose (DDD) and administration route for several medicines, including risdiplam. Risdiplam ATC and DDD are M09AX10 and 5mg, respectively. Risdiplam administrated orally.

Table S3. Interviews with patient and families' organizations (raw information)

	Country	Bangladesh	Bolivia	Indonesia	South Africa	Tunisia	Ukraine
	Geographic region	South Asia	Latin American & Caribbean	East Asia & Pacific	Sub-Saharan Africa	Middle East & North Africa	Europe & Central Asia
Treatment & Access	**Guideline**						
	Current	None	None	None	None	None	None
	Prospect	None	None	None	None	None	The Minister of Health is currently working on creating a national standard for the treatment of spinal muscular atrophy patients. Draft version is expected to be approved at the end of 2023. Nusinersen and risdiplam will appear as treatments with label limitations. Onasemnogene is expected to be included once it is recommended by HTA authorities in the country.
	Treatment						
	Evrysdi (Risdiplam)						
	Marketing Authorization	Yes	No	Yes	Yes	No	Yes
	Reimbursement	No	No	No	No	No	Yes (SMA type I)
	Access strategies	No	No	Yes (N=1)	No	No	No
	Humanitarian programs	Yes (N=3)	No	No	Yes	Yes (N=6)	No
	Importation	No	No	No	No. Patients can import medicines without registration through section 21A. However, no patient had received risdiplam through this procedure due to the high cost and the lengthy process.	No	No

Treatment & Access	**Country**	**Bangladesh**	**Bolivia**	**Indonesia**	**South Africa**	**Tunisia**	**Ukraine**
	Current	SMA patients needed to pay for risdiplam out-of-pocket. The only 3 patients that were receiving risdiplam in Bangladesh were doing it through a compassionate use program.	Risdiplam has not been available to any patient in Bolivia.	SMA patients needed to pay for risdiplam out-of-pocket since rare diseases were not publicly reimbursed. The lack of access was due to the unaffordability of risdiplam. The only patient that was receiving risdiplam was doing so because he/she participated in a clinical trial.	SMA patients needed to pay for risdiplam out-of-pocket. The only SMA patients type I that were receiving risdiplam in South Africa were doing it through a compassionate use program.	Roche was in the third and last state to get risdiplam approved in Tunisia. This decision was postponed several times due to the high cost of risdiplam. The only 6 SMA patients that were receiving risdiplam in Tunisia were doing it through a compassionate use program.	Type I SMA patients received risdiplam for free. Other SMA patients needed to pay for it out-of-pocket.
	Prospect	Patients and families' patient organizations were trying to engage with the government to get risdiplam reimbursed.	Roche was in the process of gaining registration for risdiplam.	Patient and families' organizations were trying to make risdiplam publicly reimbursed. However, the response of the Government had been negative due to SMA being a rare disease.	As SMA was not included in the prescribed minimum benefit list, SMA medicines such as risdiplam were not reimbursed. There was no evidence showing this situation will change.	Risdiplam had already been assessed by the scientific committee, and the technical committee. It was expected to be granted marketing authorization once the Ministry of Finance, the Ministry of Social Affairs, the Ministry of Health, and the Tunisian National Health Insurance Fund decided favorably.	The HTA assessment of risdiplam for the treatment of SMA patients with SMA type II started in September 2023. The assessment was expected to take 180 days.
	Spinraza (Nusinersen)						
	Marketing authorization	No	No	No	No	No	Yes
	Reimbursement	No	No	No	No	No	No
	Humanitarian programs	No	No	No	No	No	Yes
	Importation	No	No	No	No. Patients can import medicines without registration through section 21A. However, no patient had received nusinersen through this procedure due to the	No	No

	Country	Bangladesh	Bolivia	Indonesia	South Africa	Tunisia	Ukraine
					high cost and the lengthy process.		
	Situation	Nusinersen had not been available to any patient in Bangladesh.	Nusinersen had not been available to any patient in Bolivia.	Nusinersen had not been available to any patient in Indonesia.	Nusinersen had not been available to any patient in South Africa.	Nusinersen had not been available to any patient in Tunisia.	Nusinersen had been accessible in Ukraine through Biogen limited donation program during 2022-2024.
	Prospect	Biogen had shown interest in taking nusinersen to Bangladesh. However, the registration of nusinersen in Bangladesh was hampered by Biogen not having a local office in Bangladesh.	There was no evidence of Biogen trying to register nusinersen in Bolivia.	There was no evidence of Biogen trying to register nusinersen in Indonesia.	There was no evidence of Biogen trying to register nusinersen in South Africa.	There was no evidence of Biogen having an interest to register nusinersen in Tunisia.	There were ongoing conversations between the Ukrainian Government and Biogen to implement a managed access agreement for the treatment of SMA type II patients.
Treatment & Access	**Zolgensma (Onasemnogene)**						
	Marketing Authorization	No	No	No	No	No	No
	Reimbursement	No	No	No	No	No	No
	Clinical trials	No	No	No	Yes	No	No
	Humanitarian programs	Yes (N=1)	No	No	No	Yes (N=1)	No
	Importation	No	No	No	No. Patients can import medicines without registration through section 21A. However, no patient had received onasemnogene through this procedure due to the high cost and the lengthy process.	No	No
	Situation	The only person that received onasemnogene in Bangladesh did it through the global managed access program.	Onasemnogene had not been available to any patient in Bolivia.	Onasemnogene had not been available to any patient in Indonesia.	The only patients that had received onasemnogene in South Africa did it through a clinical trial conducted in the Red Cross War Memorial	The only person that received onasemnogene in Tunisia did it through the global managed access program.	Onasemnogene had not been available to any patient in Ukraine.

	Country	Bangladesh	Bolivia	Indonesia	South Africa	Tunisia	Ukraine
	Prospect	Novartis was trying to engage with the Government regarding onasemnogene abeparvovec approval.	There was no evidence of Biogen trying to register nusinersen in Bolivia.	There was no evidence of Biogen trying to register nusinersen in Indonesia.	Children's Hospital (Cape Town). There was no evidence of Biogen trying to register nusinersen in South Africa.	There was no evidence of Novartis having an interest to register onasemnogene in Tunisia.	Onasemnogene abeparvovec was on the process for gaining registration for onasemnogene.
Reimbursement	**Reimbursement system**						
	Situation	All people had insurance whether public or private. Some vaccines and essential medicines were covered by the public national insurance. However, expensive medicines were not reimbursed. There were non-mandatory private insurances in Bangladesh.	All employed people had insurance, whether public or private. Insured medicines depended highly on the insurance. Non-insured people needed to pay for their medicines out-of-pocket.	Medicines included in the National Drug Formularies list were covered by the public national insurance.	All people had insurance whether public or private. Medicines targeting diseases that were not included in the prescribed minimum benefit list were not covered by insurances.	All employed people had insurance whether public or private. The Tunisian National Health Insurance Fund was the organization responsible for reimbursement in Tunisia. They publish the fully covered medical condition list, which includes all diseases that are covered. This list is updated every 4/5 years.	All people had insurance whether public or private. Expensive and innovative medicines were reimbursed after being granted marketing authorization, and recommended by the Ukrainian HTA organization.
Best supportive care	**Best supportive care**						
	Standard of care	Yes	Yes	Yes	Yes	Yes	No
	Situation	Patients/parents needed to pay for best supportive care and the equipment out-of-pocket.	Reimbursement of the best supportive care depended on the insurance. Patients/parents needed to pay for the best supportive care completely or partially out-of-pocket. Public insurance only covered intensive therapy for SMA I patients that required constant respiratory assistance.	The best supportive care was covered by the public national insurance. However, patients/parents needed to pay for most of the equipment out-of-pocket.	Reimbursement of the best supportive depended on the insurance. Parents/patients needed to pay for the best supportive care completely (public insurance) or partially (privates) out-of-pocket. Several humanitarian groups provided the best supportive care to patients.	All SMA patients had a disability card that allows them to access best supportive care without any cost.	There was no standard of care officially approved in Ukraine. However, medical institutions followed international recommendations.

	Country	Bangladesh	Bolivia	Indonesia	South Africa	Tunisia	Ukraine
Epidemiology, Onset & Diagnosis	**Epidemiology**						
	Number	162	15	256	30	Unknown	350-450
	Source	Registry of patient organization(s).	Registry of patient organization(s).	Diagnosis center of Yogyakarta.	Registry of patient organization(s).	NA	Registry of patient organizations(s).
	Situation	Prevalence was likely to be higher due to the high rate of consanguinity and the high price of the SMA tests. In addition, Bangladesh' high rate of pneumonia deaths may have been explained by undiagnosed SMA.	Only 7 patients had a genetic diagnosis. Prevalence was likely to be higher due to the lack of knowledge about the disease in the Bolivian medical community, undiagnosis and misdiagnosis.	Data from Yogyakarta does not represent the whole SMA patient population in Indonesia. Prevalence was likely to be higher due to undiagnosis and misdiagnosis.	Prevalence was likely to be higher due to the lack of newborn screening programs.	Patients and families' organization(s) were currently working on a patient registry.	The patient registry was part of the TREAT-NMD network.
	Diagnosis						
	Newborn screening	No	No	No	No	No	Yes
	Diagnostic test						
	Reimbursement	No	No	No	Yes	No	No
	Location	Blood samples were usually sent to India, and the results were sent back in approximately 30 days. Average price for the test was $160-200.	There was a genetic center in La Paz. However, some patients went abroad to get the test.	There were three genetic centers in Indonesia: Jakarta, Bandung, and Yogyakarta. Patients could send the blood sample to the center in Yogyakarta, but the other centers required fresh blood.	Patients could get tested either in public or private hospitals. However, some patients went abroad to get the test.	There were four genetic centers in Tunisia. The average price for the tests were $20 for patients with disability card and public insurance, and $100 for patients without disability card, and without insurance.	There were numerous genetic centers in Ukraine.
	Situation	Delay in diagnosis, and unaffordability.	Undiagnosis and misdiagnosis.	Delay in diagnosis, undiagnosis, and misdiagnosis.	Delay in diagnosis.	Both patients and parents were tested for SMA.	Free as part of newborn screening, and free by individual request.

	Country	Bangladesh	Bolivia	Indonesia	South Africa	Tunisia	Ukraine
Organization, Government & Company Interface	**Government conversations**						
	Meeting(s)	No	No	Yes	No	No	NA
	Situation	A proposal had been sent to the Health Ministry and the general director of DC to recognize SMA as a rare disease, tax exemptions to companies, and to reduce prices for SMA medicines by negotiating directly with companies.	No patient and families' organizations had a legal personality, hindering possible conversations with Government.	Conversations were held. Organizations requested SMA medicines and diagnosis to be included in the National Drug Formularies list. Government was open to reimburse SMA medicines if the number of patients was significant.	NA	NA	Main interaction with the Government had been in the legal field.
	Financial relationship	No	NA	No	NA	NA	NA
	Company conversations						
	Biogen						
	Conversation(s)	Yes	No	No	Yes	No	Yes
	Nature	Short conversation. They will officially meet with Biogen, but the date had not been established. Lack of local office hampers communication.	NA	NA	In-person meeting. Biogen mentioned the biggest obstacle for SMA patients accessing nusinersen was public and private insurances.	NA	Well-developed relationship. The relationship with the national brand highly varies. The recent interaction is positive.
	Financial relationship	NA	NA	NA	NA	NA	No
	Novartis						
	Conversation(s)	Yes	No	Yes	Yes	Yes	Yes
	Nature	In-person meetings. Local offices allowed conversations to be more fluent.	NA	Patients and families' organizations requested onasemnogene to be available in Indonesia. Novartis proposed them to enroll kids in the global managed access program.	As part of the patients participating in the clinical trial in Cape Town.	Patient and families discussed with Novartis about the possibility to launch a newborn screening program for SMA in Tunisia.	Well-developed relationship. The relationship with the national brand highly varies. The recent interaction had been positive.
	Financial relationship	No	NA	No	No	Yes (sponsorship)	No
	Roche						

Country	Bangladesh	Bolivia	Indonesia	South Africa	Tunisia	Ukraine
Conversation(s)	Yes	Yes	Yes	No	Yes	Yes
Nature	In-person meetings. Local offices allowed conversations to be more fluent. Roche was advising on how to generate funds and reach its government.	Short conversation. Roche asked about several aspects to patients and families' organizations.	Patient organizations requested risdiplam to be available in Indonesia.	NA	As part of the approval of risdiplam in the country.	Well-developed relationship. The relationship with the national brand highly varied. The recent interaction had been positive
Financial relationship	No	No	No	NA	No	No

Table S4. Interview with pharmaceutical companies' consultant (raw information)

	Topic	Rationale
Treatment & Access	Registration and marketing authorization	Companies considered different criteria to market their products, i.e., governments' abilities to pay, presence of specialized clinical facilities, and trained clinicians to administer their medicines.
	Risk sharing strategies	From a payer's perspective, uncertainty and risks arises from novel and expensive medicines. Companies might install annuities, which ensured that if a patient failed to meet previously agreed milestones, the government would not be required to pay for the next installments.
	Importation of products	Companies tended to sell their products to intermediate companies to operate in non-Western markets. US pricing tended to apply.
	Clinical trials	The main challenge reported in running clinical trials for rare diseases was to enroll a significant number of patients. Thereby, it was a common practice to run a global study across countries. However, there were several obstacles to perform clinical trials in a given country, i.e., the quality of the medical facilities, and the presence of clinical experts, key opinion leaders, and commercial interests.
	Humanitarian programs	Companies prioritized countries with a low gross development product per capita and high disease prevalence to implement their humanitarian programs.
Organization, Government & Company Interface	Conversations	Patient organizations were usually consulted during the registration of a medicine and played an important role in fostering access. In certain situations, companies might request patient organizations to sue the government to make the medicine available.

Acknowledgement

Given request and permission by the president of the Ukrainian Children with Spinal Muscular Atrophy (CSMA) foundation, Vitaliy Matyushenko, I would like to personally thank for his participation in the study and for the opportunity to hear and tell the stories of SMA families and patients.

Annex

Annex 1: Search strategy

Several entries were tried in Embase:

1. 'spinal muscular atrophy'/exp AND 'low income country'/exp AND 'middle income country'/exp: 4 records were obtained.
2. ('low income country'/exp OR 'middle income country'/exp OR 'africa'/exp OR 'south and central america'/exp OR 'asia'/exp) AND 'spinal muscular atrophy'/exp AND 'health care access'/exp: 14 records.
3. ('low income country'/exp OR 'middle income country'/exp OR 'africa'/exp OR 'south and central america'/exp OR 'asia'/exp OR 'pacific islands'/exp) AND 'spinal muscular atrophy': 434 records.

The first search entry provided limited literature, while the second and the third search entries returned literature from countries not in the scope of ATMF's index due to the presence of geographical search terms that did not exclude records based on a country's income level. Therefore, low, and middle income countries in the scope of ATMF's were manually included in the search strategy.

Thereby, final search entry was:

4. ("Afghanistan" OR "Algeria" OR "Angola" OR "Armenia" OR "Bangladesh" OR "Belize" OR "Benin" OR "Bhutan" OR "Bolivia" OR "Botswana" OR "Brazil" OR "Burkina Faso" OR "Burundi" OR "Cabo Verde" OR "Cambodia" OR "Cameroon" OR "Central African Republic" OR "Chad" OR "China" OR "Colombia" OR "Comoros" OR "Congo" OR "Democratic Republic of Congo" OR "Côte d'Ivoire" OR "Djibouti" OR "Dominican Republic" OR "Ecuador" OR "Egypt" OR "El Salvador" OR "Equatorial Guinea" OR "Eritrea" OR "Eswatini" OR "Ethiopia" OR "Gabon" OR "Gambia" OR "Ghana" OR "Guatemala" OR "Guinea" OR "Guinea-Bissau" OR "Guyana" OR "Haiti" OR "Honduras" OR "India" OR "Indonesia" OR "Iran" OR "Iraq" OR "Kenya" OR "Kiribati" OR "North Korea" OR "Kosovo" OR "Kyrgyzstan" OR "Laos" OR "Lesotho" OR "Liberia" OR "Madagascar" OR "Malawi" OR "Maldives" OR "Mali" OR "Mauritania" OR "Mexico" OR "Micronesia" OR "Moldova" OR "Mongolia" OR "Morocco" OR "Mozambique" OR "Myanmar" OR "Namibia" OR "Nepal" OR "Nicaragua" OR "Niger" OR "Nigeria" OR "Pakistan" OR "Palestine" OR "Papua New Guinea" OR "Paraguay" OR "Peru" OR "Philippines" OR "Rwanda" OR "Samoa" OR "São Tomé and Príncipe" OR "Senegal" OR "Sierra Leone" OR "Solomon Islands" OR "Somalia" OR "South Africa" OR "South Sudan" OR "Sri Lanka" OR "Sudan" OR "Suriname" OR "Syria" OR "Tajikistan" OR "Tanzania" OR "Thailand" OR "Timor-Leste" OR "Togo" OR "Tonga" OR "Tunisia" OR "Turkmenistan" OR "Tuvalu" OR "Uganda" OR "Ukraine" OR "Uzbekistan" OR "Vanuatu" OR "Venezuela" OR "Vietnam" OR "Yemen" OR "Zambia" OR "Zimbabwe") AND ("Spinal Muscular Atrophy" OR "Nusinersen" OR "Onasemnogene Abeparvovec" OR "Risdiplam")

Embase

Search entry 4 was adapted to Embase. Only records that contained the selected search terms in the title, abstract and key words were searched on, resulting in the following search entry:

5. ('afghanistan':ti,ab,kw OR 'algeria':ti,ab,kw OR 'angola':ti,ab,kw OR 'armenia':ti,ab,kw OR 'bangladesh':ti,ab,kw OR 'belize':ti,ab,kw OR 'benin':ti,ab,kw OR 'bhutan':ti,ab,kw OR 'bolivia':ti,ab,kw OR 'botswana':ti,ab,kw OR 'brazil':ti,ab,kw OR 'burkina faso':ti,ab,kw OR 'burundi':ti,ab,kw OR 'cabo verde':ti,ab,kw OR 'cambodia':ti,ab,kw OR 'cameroon':ti,ab,kw OR 'central african republic':ti,ab,kw OR 'chad':ti,ab,kw OR 'china':ti,ab,kw OR 'colombia':ti,ab,kw OR 'comoros':ti,ab,kw OR 'congo':ti,ab,kw OR 'democratic republic of congo':ti,ab,kw OR 'côte ivoire':ti,ab,kw OR 'djibouti':ti,ab,kw OR 'dominican republic':ti,ab,kw OR 'ecuador':ti,ab,kw OR 'egypt':ti,ab,kw OR 'el salvador':ti,ab,kw OR 'equatorial guinea':ti,ab,kw OR 'eritrea':ti,ab,kw OR 'eswatini':ti,ab,kw OR

'ethiopia':ti,ab,kw OR 'gabon':ti,ab,kw OR 'gambia':ti,ab,kw OR 'ghana':ti,ab,kw OR 'guatemala':ti,ab,kw OR 'guinea':ti,ab,kw OR 'guinea-bissau':ti,ab,kw OR 'guyana':ti,ab,kw OR 'haiti':ti,ab,kw OR 'honduras':ti,ab,kw OR 'india':ti,ab,kw OR 'indonesia':ti,ab,kw OR 'iran':ti,ab,kw OR 'iraq':ti,ab,kw OR 'kenya':ti,ab,kw OR 'kiribati':ti,ab,kw OR 'north korea':ti,ab,kw OR 'kosovo':ti,ab,kw OR 'kyrgyzstan':ti,ab,kw OR 'laos':ti,ab,kw OR 'lesotho':ti,ab,kw OR 'liberia':ti,ab,kw OR 'madagascar':ti,ab,kw OR 'malawi':ti,ab,kw OR 'maldives':ti,ab,kw OR 'mali':ti,ab,kw OR 'mauritania':ti,ab,kw OR 'mexico':ti,ab,kw OR 'micronesia':ti,ab,kw OR 'moldova':ti,ab,kw OR 'mongolia':ti,ab,kw OR 'morocco':ti,ab,kw OR 'mozambique':ti,ab,kw OR 'myanmar':ti,ab,kw OR 'namibia':ti,ab,kw OR 'nepal':ti,ab,kw OR 'nicaragua':ti,ab,kw OR 'niger':ti,ab,kw OR 'nigeria':ti,ab,kw OR 'pakistan':ti,ab,kw OR 'palestine':ti,ab,kw OR 'papua new guinea':ti,ab,kw OR 'paraguay':ti,ab,kw OR 'peru':ti,ab,kw OR 'philippines':ti,ab,kw OR 'rwanda':ti,ab,kw OR 'samoa':ti,ab,kw OR 'são tomé and príncipe':ti,ab,kw OR 'senegal':ti,ab,kw OR 'sierra leone':ti,ab,kw OR 'solomon islands':ti,ab,kw OR 'somalia':ti,ab,kw OR 'south africa':ti,ab,kw OR 'south sudan':ti,ab,kw OR 'sri lanka':ti,ab,kw OR 'sudan':ti,ab,kw OR 'suriname':ti,ab,kw OR 'syria':ti,ab,kw OR 'tajikistan':ti,ab,kw OR 'tanzania':ti,ab,kw OR 'thailand':ti,ab,kw OR 'timor-leste':ti,ab,kw OR 'togo':ti,ab,kw OR 'tonga':ti,ab,kw OR 'tunisia':ti,ab,kw OR 'turkmenistan':ti,ab,kw OR 'tuvalu':ti,ab,kw OR 'uganda':ti,ab,kw OR 'ukraine':ti,ab,kw OR 'uzbekistan':ti,ab,kw OR 'vanuatu':ti,ab,kw OR 'venezuela':ti,ab,kw OR 'vietnam':ti,ab,kw OR 'yemen':ti,ab,kw OR 'zambia':ti,ab,kw OR 'zimbabwe':ti,ab,kw) AND ('spinal muscular atrophy':ti,ab,kw OR 'nusinersen':ti,ab,kw OR 'onasemnogene abeparvovec':ti,ab,kw OR 'risdiplam':ti,ab,kw): 183 records were obtained.

Overton

Search entry 4 was searched on Overton without variations. 773 academic and 20 grey records were obtained. In addition, the following search entry was used filtering by source countries:

6. "Spinal Muscular Atrophy" OR "Nusinersen" OR "Onasemnogene Abeparvovec" OR "Risdiplam": 32 records were obtained.

Annex 2: Interview protocol

Treatment & Access

- What's the current treatment guideline for SMA in your country? (Please provide a link if it is publicly accessible or attach to your response)
  - What is the position of spinal muscular treatments (nusinersen/onasemnogene/risdiplam) in the treatment guideline?
- How does your patient population access spinal muscular treatments (nusinersen/onasemnogene/risdiplam in the country?
  - Could you share some more information about the SMA treatments that are available in the country, if any?
  - Could you share some more information about the reimbursement system in the country?
  - Could you share some more information about the registration state/prospect of SMA treatments?
  - Could you share some more information about the market authorization state/prospect of SMA treatments?
  - Could you share any information about humanitarian programs, if any?
  - *If no medicine is available:* Could you share any information about the standard of care (best supportive care in the country)?

Epidemiology & Genetics

- How many people are affected by spinal muscular atrophy in the country?

SMA organization, Government and Company interface

- What has been the relationship or communication between your SMA patient organization and the national Government, if any?
  - If so, could you please share some information about the extent and nature of the interaction between your SMA patient organization and the national Government, if any?
- What has been the relationship or communication between your SMA patient organization and the companies Roche/Novartis/Biogen?
  - If so, could you please share some information about the extent and nature of the interaction between your SMA patient organization and the companies?

Onset & Diagnosis

- How does your patient population access spinal muscular tests in the country?
- How is your patient population typically diagnosed in the country?

Annex 3: Informed consent form

Good morning/afternoon. My name is Jorge Madrid Paredes, and I am a MSc in Drug Innovation at Utrecht University and an intern at Access to Medicine Foundation (ATMF). Thank you so much for making time for this interview.

We are gathered today to discuss the situation of access to Spinal Muscular Atrophy (SMA) treatments in your country. The objective of the study is to investigate whether the discovery of the novel medicines risdiplam, nusinersen and onasemnogene abeparvovec has improved the treatment of SMA patients in low- to middle-income countries (LMICs). As secondary objectives, the study will allow us to identify the barriers and facilitators to access to SMA treatments in LMICs. To answer this research question, interviews with various stakeholders will be conducted to determine SMA treatment access and identify impediments to access.

The interview will be conducted by researcher Jorge Madrid Paredes within his MSc in Drug Innovation at UU and his internship at ATMF. Marijn Verhoef, director of Operations and Research, may be present in the interview as supervisor of the project. The interview will take between 30 and 60 minutes, and participation is entirely voluntary. Therefore, you can exit the interview session at any time, without any negative consequences, and without providing any explanation. Data of this research will be anonymized, although information from the country in which your patient organization operates will still be present. Any publication based on this research will not include your name or any individual information by which you could be identified.

Some practical matters:

- Do you give permission to record this interview? The records will be used for transcribing and will be removed at the end of the research project.
- Before we proceed, do you have any questions about the purpose or scope of the interview?

Statement of informed consent

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions I have asked and have been answered to my satisfaction. I consent voluntarily to be a participant in this study.

Name of Participant _____

Signature of Participant _____

Date (day/month/year) _____